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Emanuel B. Schoenbach, M.D., *editor-in-chief*

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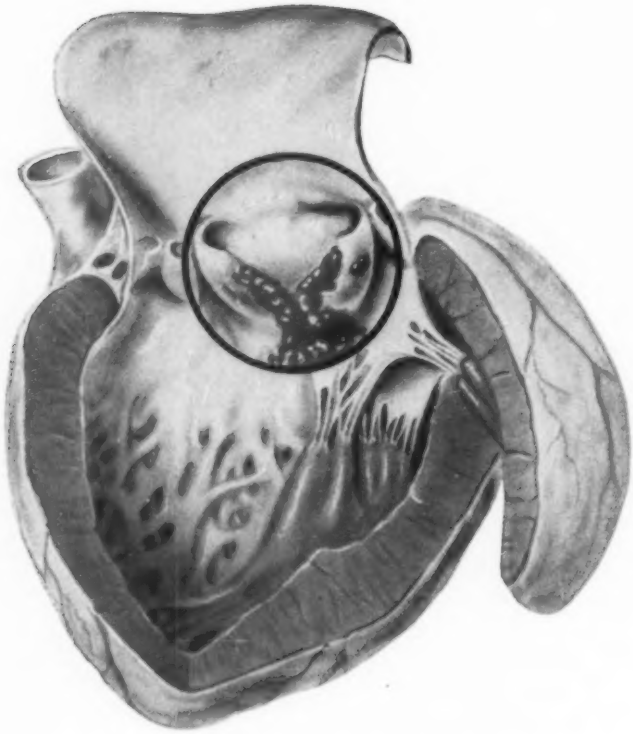

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Quarterly Review of MEDICINE

VOLUME 9 NO. 2 **MAY 1952**

FOREWORD

The QUARTERLY REVIEW OF MEDICINE is devoted to the presentation of selected abstracts encompassing the various subdivisions and related fields of internal medicine. Not only the content but the status of the material in its relationship to present-day knowledge and concept influences the basis of selection. Special review articles and advanced experimental and clinical reports on subjects of current interest are also included. It is hoped that noteworthy trends in the field of internal medicine will thus be recorded and a proper perspective on the rapidly changing and dynamic state of medical knowledge attained.

The abstracts and editorial comments are grouped together under the following headings:

INFECTIOUS DISEASES
ONCOLOGY
RESPIRATORY DISEASES
CARDIOVASCULAR DISEASES
GASTROINTESTINAL DISEASES
GENITOURINARY DISEASES
MUSCULOSKELETAL DISEASES
NEUROLOGY AND PSYCHIATRY
HEMATOPOIETIC DISEASES
ALLERGY
METABOLIC AND ENDOCRINE DISORDERS
GERIATRICS
DERMATOLOGY AND SYPHILOLOGY
DISEASES OF DOUBTFUL ORIGIN
BASIC SCIENCES
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BOOK REVIEWS
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Quarterly Review of MEDICINE

VOLUME 9 NO. 2 **MAY 1952**

Incorporating the International Record of Medicine

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MEDICINE ABSTRACTS

Infectious Diseases

Oncology

Respiratory Diseases

Cardiovascular Diseases

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Quarterly Review of **MEDICINE**

VOLUME 9 NO. 2 **MAY 1952**

Incorporating the International Record of Medicine

Current Status of Pathogenesis and Treatment of the Thrombocytopenic Purpuras

*Eugene L. Lozner, M.D.**

SYRACUSE, NEW YORK

Certain observations by various investigators within the past few years have led to the feeling that it might be desirable at this time to attempt a review of the pathogenesis and treatment of the thrombocytopenic purpuras. These observations include those by Epstein *et al* on congenital thrombocytopenic purpura,[1] those by Harrington *et al*[2] on the effects of transfusion of plasma from purpuric patients into normal subjects, those by Evans *et al*[3] on the possible relationship of idiopathic thrombocytopenic purpura to acquired hemolytic anemia, two studies of the effects of platelet transfusion into purpuric patients,[4,5] a study by Ehrlich and Schwartz[6] on the effects of splenectomy in "secondary" thrombocytopenic purpura with splenomegaly, and finally several series of patients treated by adrenocorticotrophic hormone or cortisone or both.[7,8,9,10,11,12]

CLASSIFICATION

The thrombocytopenic purpuras may be divided into three categories, the idiopathic variety (etiology unknown, Werlhof's disease, primary thrombocytopenic purpura, essential thrombocytopenic purpura), the toxic or allergic variety (in which a drug or chemical or antigen can be definitely implicated), and the secondary or "symptomatic" variety (in which the thrombocytopenia is just one manifestation of *either* a disorder of the *bone marrow* such as leukemia, aplastic anemia, pernicious anemia, chronic hypochromic anemia, tuberculosis, carcinomatosis, and lymphomatosis in which the megakaryocytes of the marrow are mechanically displaced *or* a disorder of the *spleen* such as congestive splenomegaly with or without cirrhosis of the liver, Gaucher's disease, Felty's syndrome, lymphomatosis, tuberculosis, disseminated lupus erythematosus, and sarcoid in which the

* The Department of Medicine, State University of New York at Syracuse, College of Medicine.

megakaryocytes of the marrow are present in normal or even in increased numbers).[13] To all these varieties should be added the very rare disorder, "thrombotic thrombocytopenic purpura," characterized by widespread platelet thrombi in capillaries and which thus far has been uniformly fatal.[14] This latter disease bears no clear-cut relationship to any of the other forms of thrombocytopenic purpura.

PATHOGENESIS

Although idiopathic thrombocytopenic purpura is one of the less common varieties in this group of disorders, it has attracted much attention both with regard to theories of pathogenesis and treatment ever since Kaznelson suggested splenectomy for this condition in 1916.[15] Two major schools of thought with regard to the pathogenesis of idiopathic thrombocytopenia were introduced during the years of 1915 to 1917 and have persisted to date. In 1915, Frank[16] suggested that the spleen in some way or other inhibited the formation of platelets from the megakaryocytes in the bone marrow. Kaznelson[15] and Hess,[17] on the other hand, postulated that the spleen was actually destroying the platelets at an excessive rate. Frank's hypothesis is supported by the morphologic observations of the bone marrow by Dameshek and Miller[18] and by those studies which showed that an extract of the spleen in patients with purpura was capable of producing thrombocytopenia in experimental animals.[19] These latter studies could not be confirmed by other workers.[20,21] Kaznelson's theory is at the present time supported by morphologic observations of the spleen by Doan and his co-workers.[22] The recent observations referred to in the introduction[1,2,3,4,5] actually support neither of the above theories in a clear-cut fashion. For example, Epstein[1] in a study of congenital thrombocytopenic purpura observed seven pregnancies occurring in five mothers with thrombocytopenia, three of whom had been splenectomized prior to these observations. All of five children born to the splenectomized mothers were thrombocytopenic at birth and remitted spontaneously within a few months. Of two children born to the non-splenectomized mothers, one was thrombocytopenic at birth. A review of the literature by these authors revealed that transient thrombocytopenia occurred in the majority of infants born to mothers with thrombocytopenia, whether or not the spleen of the mother had been removed prior to or during the pregnancy. It is apparent that some "humoral substance" is transferred across the placenta into the fetal circulation which results in thrombocytopenia of the newborn. It is also evident that this substance in the mother's circulation is independent of the presence or absence of her spleen. The nature and mechanism of action of such a hypothetical substance remain essentially unknown, but both hormones and antibodies are distinct possibilities. Hormones are suggested by the well-known clinical observation that idiopathic thrombocytopenic purpura in adults is almost exclusively a disease of females. A recent study[23] of some 400 patients with this disorder, 16 years of age and older, showed a ratio of females to males of almost 4 to 1. Purpura has also been observed in a few patients following large doses of estrogen.[24] The existence of a "humoral substance" is also indicated by the study of Harrington and co-workers[2] who transfused blood or plasma from patients with thrombocytopenic purpura into non-thrombocytopenic subjects. In blood or plasma from

eight of ten patients with idiopathic thrombocytopenia, a factor could be demonstrated which decreased promptly the platelet count of the recipients with the thrombocytopenic effect persisting for from five to seven days. Five of the patients had this factor present in their plasma after their spleens had been removed. In two of these patients the factor was present even after their own platelet counts had returned to normal. It is of interest that one of the recipients showing a thrombocytopenic effect had had his spleen removed previously. The exact significance of these observations with regard to the pathogenesis of the disease is not clear, but this avenue of study is certainly an attractive one to pursue. The case for the existence of a thrombocyte auto-antibody has recently been presented by Evans and his associates,[3] who were able to demonstrate a platelet-agglutinating factor in the serum of some of their patients with idiopathic thrombocytopenia. These workers have also called attention to the occasional co-existence of acquired hemolytic anemia and thrombocytopenic purpura and to the presence of a positive anti-globulin (Coomb's) test in some patients with idiopathic thrombocytopenia without anemia.

Two sets of observations on the survival of platelets transfused into patients with thrombocytopenia have recently been reported.[5,6] Both sets of workers agree that platelet disappearance in the recipient may be extraordinarily rapid when the recipient has "acute idiopathic thrombocytopenic purpura." However, when the recipient has either the more chronic form of this disease or thrombocytopenia associated with acute leukemia or aplastic anemia, platelet survival time may be significantly longer. One interpretation of these results is that, when platelet survival time is short, the pathogenesis of the original thrombocytopenia was most probably an increased rate of destruction of platelets. On the other hand, when platelet survival time is long, decreased production of platelets may be the chief pathogenetic mechanism.

It has been known for many years that one of the frequent accompaniments of thrombocytopenia is increased vascular or capillary fragility as demonstrated either by the application of a suction cup or by inflating a sphygmomanometer on the upper arm to a pressure below arterial pressure. We have preferred the latter technic using a standard test of 100 mm. of mercury for 10 minutes and counting the petechiae in a 2.5 cm. diameter circle on the forearm 4 cm. below the antecubital crease. The nature of the mechanism of this vascular fragility is as obscure as that of the original thrombocytopenia. That thrombocytopenia may occur without vascular fragility is well-known also. Bedson[25] has shown experimentally that the injection of an agar-serum in animals produces thrombocytopenia without purpura. However, when such an injection is preceded by an injection of "anti-red cell serum," the more usual syndrome of thrombocytopenic purpura results. In this regard, Macfarlane[26] has called attention to the clinical phenomenon that splenectomy may improve capillary fragility without altering the number of platelets. This line of study has been pursued by Robson,[27] who observed that the vascular defect in purpura was improved by splenectomy very soon after the surgery and long before any increase in platelets could be observed. In fact, even before the advent of the adrenal steroids, he ventured the hypothesis that the early changes might be a nonspecific effect of operative interference.[27] With the increased

availability of various hormones, Robson[8] was able to show that adrenocortical activity was indeed related to capillary resistance. Faloon and co-workers[9] confirmed these observations and showed that ACTH and cortisone regularly improved the vascular defect in thrombocytopenic purpura regardless of etiology but only irregularly increased the platelet count and then only after several days following the improvement in vascular fragility.

Within recent years the nature of the coagulation defect in thrombocytopenia has been elucidated to a considerable extent. For some time previously it had been standard teaching that the clotting time in thrombocytopenia was normal and that there was essentially no coagulation defect other than that of a rather poor clot retraction associated with low platelets. The error of this concept was clearly demonstrated by Quick and associates[28] who showed that beyond any question there is much slower conversion of prothrombin to thrombin in the absence of platelets than in normal blood. Thus, in thrombocytopenia, although there is sufficient conversion of prothrombin to result in an essentially normal venous coagulation time as this test is ordinarily performed, when the prothrombin content of the resultant serum is measured, it is found to be significantly higher than that of serum after the clotting of normal blood. These observations have been confirmed by many workers.[29,30]

A much more controversial observation is that of Allen[31] who presented some evidence in favor of the existence of a heparin-like substance in the blood of some patients with thrombocytopenia, a substance which was allegedly responsible for a coagulation defect and which could be "neutralized" by the administration of toluidine blue or protamine sulfate. Unfortunately this work has been rather irregularly confirmed, and both the primary hypothesis of a heparin-like substance and the therapeutic usefulness of the above substances remain shrouded with considerable doubt and skepticism. Our laboratory has been unable to confirm either observation.

TREATMENT

Needless to say, the keystone of treatment is diagnosis, and in these disorders it is imperative to come to some sort of conclusion concerning the category into which the thrombocytopenia is thought to fall. A most careful history, physical and laboratory examination including a morphologic study of the bone marrow and lymph nodes, should these appear suspect, are essential in this diagnostic survey. If drugs or allergens appear implicated, these should be eliminated and conservative management including transfusions allowed to prevail. If the spleen is enlarged, the likelihood of the patient having idiopathic thrombocytopenic purpura is minimal, and the work of Ehrlich and Schwartz[6] should be considered. These investigators showed that, when splenomegaly occurs with thrombocytopenic purpura, leukopenia is a rather constant finding. They also showed that in "secondary thrombocytopenic purpura," when the marrow showed a normal or increased number of megakaryocytes, splenectomy was "as effective" therapeutically as in idiopathic thrombocytopenic purpura. Of course, when the marrow shows such pathology as leukemia, aplasia, tuberculosis, lymphomatosis, carcinomatosis, or megaloblastic arrest, splenectomy is rarely to be considered.

The therapy of "idiopathic thrombocytopenic purpura" presents a more complicated problem. Age is very definitely a factor in the decision with regard to treatment. Newton and Zuelzer[32] have recently reviewed their experience with 47 children with this disease and conclude that the majority of children show a marked tendency to spontaneous and complete recovery. They, as well as many others, feel that splenectomy in childhood should be reserved for uncontrollable bleeding or for very chronic and recurrent purpura. They also point out that in such situations splenectomy results in "cures" in only about half the patients. In view of the recent experiences with hormonal therapy, there may be even less indication for splenectomy than these authors indicate.

In adults with idiopathic thrombocytopenic purpura, the problem is also the one of expectant or conservative management (with or without the use of transfusions and hormones) versus splenectomy. Here too, as in childhood, there is a certain tendency to spontaneous and complete remission, but most series indicate that only about one third of adults will have such a remission.[33] In this regard, Hirsch and Dameshek[34] have attempted recently to differentiate "acute self-limited thrombocytopenia," in which there is spontaneous recovery in less than 4 months, from "chronic idiopathic thrombocytopenia," in which thrombocytopenia persists and where splenectomy seems to offer a chance of permanent cure in about two thirds of the patients. However, this type of differentiation is comparable to a definition in which the word defined is used in the definition. What Hirsch and Dameshek appear to indicate is the wisdom of delaying splenectomy for at least four months in most patients with a purpura which is not fulminating in nature. The chief argument against such a delay is the constant menace of a cerebrovascular accident in these patients. Against this menace must be weighed the operative mortality of splenectomy and the possibility that splenectomy will afford either incomplete relief or none at all in one third of the patients. Obviously the decision is not an easy one. Of some help while deliberating this decision is the now proven value of ACTH and cortisone. Bethell,[7] Robson,[8] Faloon,[9] Wintrobe,[10] Evans,[11] and Jacobson[21] have reported series of varying numbers treated with these hormones. All of these observers have reported some success but the completeness and permanence of this success have not been constant. There can be no doubt that these hormones are of definite value in the handling of fulminating emergencies particularly menorrhagia. We have had somewhat more success with ACTH than cortisone in these situations, and large doses have been usually required. We have also had moderate success with these hormones in the hemorrhagic emergencies due to the thrombocytopenia associated with acute leukemia and aplastic anemia.

Also of value in the treatment of thrombocytopenic purpura, while deliberating splenectomy, is the use of transfusions, most particularly those of platelet-rich polycythemic blood with siliconized apparatus.[4] Although in most patients the remission so obtained is quite transient, two patients have been reported in whom a sustained remission followed the transfusion.[4] In this situation as in so many others in medicine, the possibility of coincidence cannot be eliminated. Unfortunately, most hospitals are not equipped to transfuse polycythemic blood in siliconized apparatus due to the unavail-

ability either of donors or of the equipment. In such cases the patient will be benefited chiefly by the replacement of blood lost by hemorrhage.

There are a few patients with idiopathic thrombocytopenic purpura who are completely refractory to all forms of therapy including transfusions, hormonal treatment, and splenectomy. When such are women in whom the chief situation threatening life is metrorrhagia, x-ray castration, androgen therapy, and even hysterectomy may be considered. Certainly the last mentioned fits in the category of heroic measures and should only be considered as a last resort. Fortunately, such patients constitute an extremely small percentage of patients with thrombocytopenic purpura.

SUMMARY

1. The recent literature concerning pathogenesis and treatment of the thrombocytopenic purpuras has been reviewed.

2. The greatest advances have been achieved in the understanding of the hemostatic defects in idiopathic thrombocytopenic purpura.

3. The most recent evidence in this disorder favors the existence of a humoral substance which is in the blood and does not require the presence of the spleen and which is capable of depressing the platelet count of babies by transplacental transfer or of subjects into whom it is transfused.

4. There is also evidence that the capillary fragility usually associated with thrombocytopenia may be improved by adrenocortical hormones.

5. The treatment of idiopathic thrombocytopenic purpura in children should probably be expectant.

6. The treatment of idiopathic thrombocytopenic purpura in adults should probably first be expectant with or without the use of transfusions (preferably of platelet-rich blood with siliconized apparatus) and with or without the use of ACTH and cortisone for hemorrhagic emergencies. Splenectomy is indicated in adults when megakaryocytes are present in adequate numbers in the marrow and when expectant management appears to menace the life of the patient. Splenectomy, however, results in a "cure" in only about two thirds of all patients with idiopathic thrombocytopenic purpura.

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On February 8th, the National Multiple Sclerosis Society launched a public drive to raise $425,000 for 1952. It is planned that more than half of the money raised will be spent on research, the remainder going toward education and service to physicians, patients, and the public. An emphasis on research has been made because an effective treatment for MS is yet to be found.

A vital part of the Society's research program has been the establishment of seven clinics which are specialized research and treatment centers. At the MS clinics, diagnosis is made, treatments which may be helpful are given, and in some centers rehabilitation treatments are offered. These clinics are located at NYU-Bellevue Medical Center, New York City; Montefiore Hospital, New York City; Massachusetts General Hospital, Boston, Mass.; Boston State Hospital, Boston, Mass.; Detroit Memorial Hospital, Detroit, Mich.; Snyder-Jones Clinic, Winfield, Kansas; and Cedars of Lebanon Hospital, Los Angeles, Calif.

The Society believes that patients must live with MS to the best of their capacities. To help effectuate this, it has published a rehabilitation manual for physicians designed to guide physicians in a home care program for patients through physiotherapy. Members are kept informed of all developments and progress through its official bulletin, AARMS FORWARD. A medical manual for physicians, keeping them informed of all developments and information in the field, has been widely distributed. A Panel of International Corresponding Neurologists, consisting of 56 neurologists from 26 countries, has been established to keep active research centers and investigators in the world posted on developments in the field.

Recent reports indicate that the life expectancy in MS is not much less than that of the normal population, but living with MS requires courage and great effort on the part of patients who have to cope with it for many years. They have received hope and encouragement as a result of the efforts of the Society to conquer MS. In its current drive, the Society is asking the public to send contributions to MS, 270 Park Avenue, New York City.

Present Status of Penicillin Prophylaxis of Rheumatic Fever*

Benedict F. Massell, M.D.

BOSTON, MASS.

Rheumatic fever is a repetitive disease in which each new episode may increase the degree of cardiac damage. Most deaths from rheumatic heart disease, especially in children and young adults, are traceable directly to recurrences of active rheumatic fever, the mortality from first attacks being relatively low. Therefore, the problem of rheumatic fever prevention can be divided into two phases: the first is concerned with the prevention of initial attacks; the second involves the prevention of recurrences of the disease.

It is now well established that practically all initial and recurrent attacks of the disease are precipitated by antecedent hemolytic streptococcal respiratory infections. The demonstration of the role of the hemolytic streptococcus is of considerable practical importance as well as of theoretical interest, since it allows one to approach the problem of rheumatic fever prevention through an attack on the hemolytic streptococcus.

Penicillin may be used in two ways for the prevention of rheumatic fever. One method depends upon the prevention of hemolytic streptococcal infections by the continuous daily administration of oral penicillin. The other involves the prompt treatment of hemolytic streptococcal respiratory infections with adequate doses of penicillin.

CONTINUOUS DAILY ORAL PENICILLIN

The method of continuous daily oral penicillin is aimed at the prevention of rheumatic fever by the prevention of hemolytic streptococcal infections. It is especially applicable to the problem of preventing rheumatic fever recurrences in individuals who have had one or more previous attacks of the disease.

Rationale. Data regarding the possible value of oral penicillin for the prevention of hemolytic streptococcal respiratory infections have been obtained indirectly from observations on the effect of oral penicillin on the throat flora of persons found to be carriers of hemolytic streptococci. The carrier studies indicate that hemolytic streptococci can be completely cleared from the throat by oral administration of penicillin in about three fourths of the individuals found to be harboring the organisms. Even in those in whom the streptococci are not permanently eradicated, the organisms are greatly suppressed, so that cultures usually fail to reveal their presence during the period that penicillin is being administered (see table I).

It seems reasonable to infer that a procedure which will greatly check or eradicate hemolytic streptococci which already have gained a foothold in the pharyngeal mucosa will also prevent the implantation of new strains that have not yet obtained such a foothold but to which the patient may be exposed. Thus far, during the past five years,

* Reprinted from Med. Concepts Cardiovas. Dis. *20*:108-09, September, 1951 (published by the American Heart Association).

these inferences have been borne out by our experience at the House of the Good Samaritan where, among a limited number of patients who have recovered from previous rheumatic fever and who have been carried on a regimen of daily oral penicillin, we have not yet encountered a single instance of hemolytic streptococcal respiratory infection or of rheumatic fever recurrence.

Dosage. On the basis of the carrier studies, it would appear that 100,000 to 200,000 units of oral penicillin three times daily is an effective schedule. For most of our patients on the prophylactic regimen, we have actually used only 100,000 units at each dose, but in relatively few patients, all of whom have weighed over 100 pounds, the individual dose has been 200,000 units. At the present time, we are studying the possible effectiveness of oral penicillin in less frequent doses, but, as yet, do not have sufficient data to warrant recommending that the penicillin be administered any less often than three times daily.

TABLE I

Cultures Positive for Hemolytic Streptococci Prior to and During Oral Penicillin Therapy[a]

	Total Cultures	Positive for Hemolytic Streptococci	
		Number	Percentage
Prior to therapy	229	183	80
During first 24 hours	33	8	24.2
During second 24 hours	34	2	5.9
Between third and last day	235	5	2.1

[a] Exclusive of non-group-A strain with penicillin sensitivity of 5 to 10 units.

The first dose is given when the patient awakens in the morning and the last dose just before he goes to bed at night. For children who are attending school, the midday dose is given on arrival home from school. Since food interferes with the absorption of oral penicillin, it is important that each dose of the antibiotic be given at least one-half hour (preferably one hour) before meals and at least two hours (preferably three hours or more) after meals.

RISKS AND DISADVANTAGES

The only important risk of daily oral penicillin is the possible development of a hypersensitivity (allergic) reaction. Such reactions fortunately occur infrequently and are rarely serious. Penicillin allergic manifestations may include fever and joint pains and may cause a mistaken diagnosis of rheumatic fever recurrence. However, the penicillin reaction is almost always accompanied by marked urticaria, whereas urticaria is rarely, if ever, a manifestation of rheumatic fever. If a penicillin reaction does not occur within the first two weeks after beginning the prophylactic regimen, it is not likely to occur subsequently, especially if the penicillin is taken every day without periods of interruption.

Another possible danger to be considered is the development of penicillin-resistant organisms in the throat flora of persons on the prophylactic regimen. Although the general level of penicillin resistance of many throat flora strains is actually elevated by the administration of penicillin, the change does not involve the hemolytic streptococcus. In fact, the development *in vivo* of penicillin resistant group A hemolytic streptococci under any circumstances has not as yet been reported. Furthermore, the degree of

resistance acquired by the other organisms of the throat flora in persons receiving 100,000 to 200,000 units of oral penicillin three times daily is not sufficiently great to preclude the effective penicillin treatment of an infection which subsequently might be caused by one of these more resistant strains.

Some persons consider that taking three tablets every day and taking precautions to prevent the penicillin from mixing with food in the upper gastrointestinal tract is a nuisance. The value of daily penicillin prophylaxis for the individual known to be susceptible to rheumatic fever far outweighs this objection.

A fourth objection to the prophylactic penicillin regimen is its cost; at present prices, it amounts to about $100 per year.

Indications. As previously stated, continuous daily oral penicillin is especially applicable to individuals who have had one or more previous attacks of definite rheumatic fever. If the patient is a child, the prophylactic regimen probably should be continued through the end of the period of schooling, that period in life when exposure to the hemolytic streptococcus is likely to be the greatest. In adults, the regimen probably should be continued for at least five years from the last attack of rheumatic fever. For other adults with rheumatic heart disease who do not fall within the latter category, prophylactic daily penicillin is sometimes also indicated when circumstances enhance exposure to hemolytic streptococcal infections.

A continuous prophylactic regimen is not indicated for individuals who have not had definite rheumatic disease. However, for the child who comes from a rheumatic family, continuous daily oral penicillin is indicated for limited periods when there is known exposure to hemolytic streptococcal infection.

PENICILLIN TREATMENT OF HEMOLYTIC STREPTOCOCCAL INFECTIONS

Prompt penicillin treatment of all hemolytic streptococcal respiratory infections, as a prophylactic measure, is especially applicable to the problem of preventing initial attacks of rheumatic fever. Since about 50 per cent of hemolytic streptococcal infections are either subclinical or so mild that they are not readily recognizable, this method of prophylaxis should not be substituted for the more reliable method of continuous daily oral penicillin in individuals who have had a previous attack of definite rheumatic fever.

Rationale. Although not recommending penicillin therapy of streptococcal infections as the method of choice for preventing rheumatic fever in individuals who have had previous attacks, nevertheless, through a study of such subjects at the House of the Good Samaritan we were first able to demonstrate the efficacy of this method. Thus, among a group of 34 authentic rheumatic subjects proven clinical, hemolytic streptococcal respiratory infections treated with large doses of penicillin for ten days were followed by rheumatic fever recurrences in only 2 instances (6 per cent); whereas among 12 comparable rheumatic subjects, similar streptococcal infections not treated with penicillin were followed by definite rheumatic fever recurrences in 6 instances. The latter figure is consistent with the average recurrence rate following hemolytic streptococcal infections observed by us at the House of the Good Samaritan during the pre-penicillin era.

If penicillin treatment of hemolytic streptococcal infections suppresses the growth

of streptococci in the upper respiratory tract sufficiently to reduce the elaboration of the unknown rheumatic fever-producing substance to subeffective levels in persons who have previously had one or more attacks of rheumatic fever and who are presumably vulnerable to the disease, it seems reasonable to expect that similar treatment would have a similar effect in individuals who may be susceptible to rheumatic fever but who have not yet had a previous attack. The validity of this inference is supported by the studies of Denny and his associates, who observed in an air force training station only 2 cases of definite rheumatic fever in 798 young men with streptococcal infections treated with penicillin in contrast to 17 definite attacks of the disease in 804 untreated patients.

Application and Dosage. In the application of penicillin therapy of hemolytic streptococcal respiratory infections to the therapy of preventing initial attacks of rheumatic fever, the following suggestions are offered as a guide:

1. All persons, particularly those between the ages of 5 and 25 years, must be considered to be possibly susceptible to rheumatic fever. Individuals who come from rheumatic families are especially likely to be vulnerable.

2. All illnesses with a temperature of 101°F. or higher, especially if there are accompanying respiratory manifestations, should be considered to be possible hemolytic streptococcal infections until proven otherwise and should be treated with penicillin.

3. The patient or his parents must be instructed in the importance of getting therapy started promptly; if possible, within 24 hours of onset of clinical symptoms.

4. Failure of a fever to respond to penicillin therapy within forty-eight hours is evidence that the illness is not due to hemolytic streptococcus and is an indication for a change in therapy.

5. When a febrile illness responds within forty-eight hours to penicillin therapy, the treatment should be continued for a total period of at least ten days. Discontinuation of therapy too early in instances of hemolytic streptococcal infection often results in a subclinical or clinical relapse.

6. Penicillin must be administered in a practical yet effective manner. The following routine is suggested:

First three days: Intramuscular procaine penicillin, 300,000 units once daily, or oral penicillin 300,000 units four times daily.

Next two days: Oral penicillin, 200,000 units three times daily.

Last three days: Oral penicillin, 100,000 units three times daily.

If oral penicillin should be used throughout the ten day period of therapy, the total amount required for the recommended regimen would be seventy-five tablets of 100,000 units each. This amount of penicillin can be purchased for approximately $7.50.

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ABSTRACTS

infectious diseases

72. *Cortisone Treatment of Trichinosis.* EDGAR ROSEN, Oakland, Calif. Am. J. M. Sc. *223*:16-19, January 1952.

Cortisone therapy was employed in a moderately severe case of trichinosis, and appeared to be of striking benefit. A 42 year old man was hospitalized because of a two week febrile illness suggestive of trichinosis, and this diagnosis was established by a muscle biopsy which showed recent infestation. During a preliminary control period the patient remained febrile and complained of severe muscular aching as well as associated systemic symptoms. Rapid defervescence and dramatic symptomatic improvement then occurred when cortisone treatment was initiated. In order to establish a second control period, the drug was withheld after a four day course, and this was followed by clinical relapse. Remarkable benefit again appeared to result from the resumption of cortisone therapy. This was continued for 14 days, after which the patient remained asymptomatic. During the periods of cortisone administration the reduction in circulating eosinophils was gradual and lagged considerably behind the clinical response. Another observation of some interest was the failure to obtain a positive skin reaction to trichinella extract until after cortisone had been discontinued. It appeared that cortisone effectively suppressed the manifestations of active disease in this patient, probably by altering the host reaction to the invading trichinae. 6 references. 1 figure.—*Author's abstract.*

73. *World Distribution and Trend of Cerebrospinal Meningitis since 1939.* MATTHIEU JEAN FREYCHE, M.D. World Health Organization, Epidemiological and Vital Statistics Report, *4*:309-31, August-September, 1951.

The world incidence of cerebrospinal meningitis from 1939 to 1950 is documented. For the past 20 to 30 years the disease has occurred at a high rate of incidence in North Africa and at present it prevails in epidemic proportions. The relationship between morbidity and mortality is presented. It is difficult to draw any conclusions as to the effects of chemotherapy or chemoprophylaxis from such epidemiologic studies. There appears to be variation in case morbidity with advanced epidemics. The relationship to climate and environmental factors is found to be quite complex, and some of the simple explanations for periodicity in the northern hemisphere are insufficient to account for the observations in North Africa and other equatorial countries. 8 references. 6 figures. 8 tables.—*Emanuel B. Schoenbach, M.D.*

74. *Neomycin in the Treatment of Human Amebiasis.* LEON V. MCVAY, JR., RAYMOND L. LAIRD AND THOMAS N. STERN, Memphis, Tenn. Am. J. M. Sc. 223: 20-24, January 1952.

The action of neomycin in human amebiasis was investigated *in vitro* and its clinical application was studied in 8 patients. This antibiotic, produced by a species of *Streptomyces fradiae* and closely related to streptomycin and streptothricin, had previously been noted to alter the intestinal flora. Shortly after this study was begun, Kadison and his associates reported the *in vitro* amebicidal action of neomycin.

In vitro sensitivity studies using a strain of *E. histolytica* revealed no amebae present at the end of 48 hours in the presence of 500 to 1000 units of neomycin per cubic centimeter of overlay. The number of amebae was greatly reduced with as little as 100 units per cc.

Eight patients with mildly symptomatic amebic colitis were treated with neomycin. Three of six patients treated with 1,600,000 units of oral neomycin over a seven day period remained asymptomatic and free of amebae for 3 months. Positive stools were again found in the remaining 3 patients. These were retreated with 4,800,000 units of neomycin; no recurrence has been noted in 3 months in these patients. Two additional patients treated for 12 days with 4,800,000 units have been ameba-free for one month.

In one patient a transient azotemia and albuminuria was noted; this disappeared within 72 hours after cessation of treatment. Three patients had mild painless diarrhea and 2 complained of minimal nausea. A striking increase in yeast cells was found in the stools of every patient receiving neomycin. 19 references.—*Author's abstract.*

75. *Tuberculosis Attack and Death Rates of Household Associates. The Influence of Age, Sex, Race, and Relationship.* RUTH R. PUFFER, L. D. ZEIDBERG, ANN DILLON, R. S. GASS AND R. H. HUTCHESON, Nashville, Tenn. Am. Rev. Tuberc. *65*:111-27, February 1952.

In the Williamson County Tuberculosis Study, household associates of persons with tuberculosis (termed index cases) have been placed under observation and followed closely by examinations in the clinic and by visits of public health nurses. Since the establishment of the Study in December, 1931, 767 households have been investigated and followed. Of these 767 households, 298 (38.9 per cent) had a "sputum-positive" or fatal index case. The analyses reported in this paper are limited to the experience of the 1,358 household associates of these 298 "sputum-positive" index cases with an evaluation of the factors, age, sex, race, and relationship.

The method of analysis is the same as that developed by Frost and used in previous publications. Tuberculosis attack rates were obtained by dividing the number of new cases which developed during the period of observation by the "person-years" of observation and multiplying the quotient by the unit 1,000. A person-

year is one person followed for one year and is used to replace population. In the calculation of death rates, person-years replace population in the denominator.

The tuberculosis attack rate for the Negro associates (9.2 per 1,000 person-years) was higher than for the white associates (5.5 per 1,000 person years). A variation was noted by age groups. The highest attack rates were observed in white females in young adult life, 15 through 34 years of age, and in Negro females at a slightly earlier period, from 10 through 24 years of age.

The number of deaths from all causes of these household associates was greater than expected, based on the death rates in Tennessee. Seventy-seven deaths were observed in the white associates while 64 were expected; 75 deaths were observed in the Negro associates while 49 were expected.

The attack and death rates for the close relatives (parents, siblings and children) living in these households were found to be higher than the rates for other members of the households. The tuberculosis death rates for the close relatives (308.9 for the white and 934.4 per 100,000 person-years for the Negro) were much higher than the rates for other household members (81.8 for the white and 409.5 per 100,000 person-years for the Negro), and the latter rates were higher than those in the general population of Tennessee (58.4 for the white and 152.2 per 100,000 population for the Negro).

The evidence presented indicated that age, sex, race and genetic relationship determine the development of tuberculosis in persons exposed to "sputum-positive" index cases. These factors should be considered in the development of a tuberculosis control program and also in guidance of research. The genetic factor, as well as exposure to tubercle bacilli, is responsible for high attack and death rates. 16 references. 6 figures. 9 tables.—*Author's abstract.*

76. *A Comparative Study of the Hemagglutination Test for Antibodies and Its Hemolytic Modification in Tuberculosis.* MOLLIE MOLLOY AND THADDEUS J. KOTT, Jamaica, N. Y. Am. Rev. Tuberc. 65:194-200, February 1952.

In 1948, Middlebrook and Dubos described a specific hemagglutination test which employs the use of washed sheep erythrocytes sensitized with aqueous extracts of tubercle bacilli. These sensitized erythrocytes are rendered agglutinable by specific antibodies. Smith and Scott substituted a special old tuberculin, four times the standard strength for the aqueous extract. In 1950, Middlebrook reported a modification of this test wherein complement is added to the reaction system, thereby making it a test of hemolysis rather than one of hemagglutination. A comparison study was made of both tests. The preparation of the materials and the technique of the hemagglutination reaction and the hemolytic modification were essentially as described by Middlebrook and Dubos, with a few modifications as described. One hundred tuberculous and 88 nontuberculous cases were studied. Among the tuberculous cases 31 per cent of the hemagglutination tests and 35 per cent of the hemolytic tests showed a titer of 1:4 or less. Among the nontuberculous cases, 70 per cent showed an agglutination titer and 96 per cent a hemolytic titer of 1:4 or less. The tuberculous cases showed agglutinin titers ranging from

0 to 1:256 and the hemolytic titers from 0 to 1:1,024; whereas with the nontuberculous sera the hemagglutinin titers range from 0 to 1:32 and the hemolytic titers from 0 to 1:16. It seems significant that among the nontuberculous cases 20 per cent were completely negative by hemagglutination but, in contrast, 90 per cent by hemolytic test. The hemolytic test appears to be more specific than the hemagglutination test, but as yet, not sufficiently or selectively sensitive. There is a lack of correlation between the two tests. It is suggested that the antibodies which are measured in the two tests are different. It appears that the hemolytic modification is the more promising test as a possible diagnostic tool for case finding. 7 references. 4 tables.—*Author's abstract.*

77. *Explosive Outbreak of an Atypical Pneumonia ("K-8 Fever").* LT. PHILIP TROEN, U. S. Army Reserve. A. M. A. Arch. Int. Med. *89*:258-69, February 1952.

Forty-five cases of atypical pneumonia occurred at an Army Hospital in Kobe, Japan; 25 were patients in the hospital at the time of the occurrence of the outbreak, most of them evacuated from Korea, and the remaining 20 were members of the staff of the hospital. These cases were highly similar clinically and roentgenographically. The most frequent symptoms were fever, chilly sensations, malaise and chest pain, a non-productive cough, headache, anorexia and myalgia occurred in nearly two thirds. Stiffness of the neck occurred in 11 patients; a skin eruption was an initial symptom in 2 patients and occurred later in 7 other patients. The liver was enlarged in 10 patients, and in 4 of these the spleen also became enlarged; one other patient showed enlargement of the spleen alone. Physical findings in the examination of the chest were few, chiefly rales, but roentgenological examination showed pulmonary involvement, ranging from small patches to large hazy densities; both lungs were involved in 34 patients, and one lung in 10 patients; no positive roentgenogram was obtained in one patient. There was no definite correlation between the extent of the pulmonary involvement and the severity of the constitutional symptoms, fever, etc.; also there was no correlation between the extent of the pulmonary involvement and its duration as shown by roentgenograms. Fifteen patients were treated with aureomycin, 7 with penicillin, 8 with both of these antibiotics, 3 with chloramphenicol and other combinations; 12 were not given antibiotics. There was no evidence that any antibiotic was of benefit in any of these cases; it is also noted that the disease developed in 2 patients under penicillin treatment for syphilis, and in another patient while taking aureomycin for tonsillitis.

All bacteriologic studies in these cases were negative; neither a virus nor a rickettsial organism was isolated from blood clot or throat washings. Serologic studies were negative; these studies included the cold agglutination test, complement fixation tests for fever and psittacosis, and studies of influenza hemagglutination-inhibition, all of which were negative. As the cause and nature of this disease could not be determined it was named "K-8 fever" for the hospital where the outbreak occurred (Kobe Eighth Station Hospital). 2 references. 7 tables. 8 figures.

78. *Terramycin Therapy of Urinary Tract Infections.* C. RAY WOMACK, GEORGE GEE JACKSON, THOMAS M. GOCKE, EDWARD H. KASS, THOMAS H. HAIGHT, AND MAXWELL FINLAND, Boston, Mass. A. M. A. Arch. Int. Med. *89*:240-87, February 1952.

In this series of cases of urinary tract infection treated with terramycin, there were 107 patients with bacteria and pus in the urine, and 5 with symptoms of urinary tract infection and bacteria in the urine, but no pyuria. The majority of these patients were over 60 years of age and showed either systemic disease or local conditions predisposing to urinary tract infection. The organisms most frequently isolated from the urine before treatment was begun were *Escherichia coli* and *Aerobacter aerogenes;* these organisms were eliminated by the administration of terramycin in most instances. *Proteus vulgaris* and *staphylococci* were not found so frequently in the urine cultures before treatment; but, if present, they were not eliminated by terramycin. They also frequently appeared in the cultures during or shortly after treatment. Terramycin treatment resulted in clearing the urine of bacteria in 37 per cent of all cases, but in only 20 per cent of cases in which more than one organism was present before beginning treatment. These bacteriologic results showed "fairly good correlation" with the results of testing the sensitivity of the various organisms to terramycin *in vitro.* The terramycin therapy cleared up or markedly diminished the pyuria in about 50 per cent of the cases, especially in acute cases and in those in which pyuria was marked before treatment was begun. The treatment was considered to be of definite benefit in about half the cases, as judged by both laboratory and clinical findings. There were 14 deaths in this series: only 1 of the patients who died was under 60 years of age and 7 were more than 70; some of them had obstructive lesions or anatomic defects in the urinary tract, others had definite symptoms of kidney dysfunction. Frequently *Staphylococcus aureus* infection occurred during treatment, and terramycin was not effective against this organism. The toxic effects of terramycin included nausea, vomiting, and diarrhea, which were sometimes so severe as to make it necessary to discontinue treatment; this was also an important factor in the fatalities. 7 references. 9 tables.

79. *Infections with Pseudomonas Aeruginosa Treated with Polymyxin B.* ERNST JAWETZ, University of California School of Medicine, San Francisco, Calif. A. M. A. Arch. Int. Med. *89*:90-98, January 1952.

In 35 cases of infection with *Pseudomonas aeruginosa*, there were 4 cases of acute pyelonephritis, 8 cases of chronic pyelonephritis, 9 cases of wound infection, 5 cases of chronic otitis media, 3 cases of infected sinus tract, 2 cases of meningitis, 2 cases of conjunctivitis, and 1 case each of purulent arthritis and chronic maxillary sinusitis.

All cases of pyelonephritis were treated with polymyxin B given intramuscularly: in the acute cases, the dosage was 1.5 to 2.8 mg. per Kg. daily for six to eight days; in the chronic cases, 1.5 to 2.5 mg. per Kg. for six to eleven days. All the acute cases were cured; in the chronic cases, there was temporary improvement with

disappearance of the organisms, but a relapse occurred in all. In the cases of wound infection a polymyxin B solution of 1 mg. per ml. was instilled into the wound and also used for continuous wet dressings; in 8 cases the organisms were eradicated and the wound healed well; in 1 case the treatment was not effective.

The 5 cases of chronic otitis media were treated by instillation of the same solution four times a day for six days. In all these cases the infection cleared up and the discharge ceased. In the 3 cases of infected sinus tract, instillation of the polymyxin B solution cleared the infection with healing of the sinus in 2 cases; in the third case a superinfection with *Proteus vulgaris* occurred.

In the 2 cases of meningitis, 5 mg. of polymyxin B was given intrathecally daily for four days then every two days for two to three weeks. One of these patients was cured without sequelae; the other, who was treated late, developed hydrocephalus although the cerebrospinal fluid was sterilized. The 2 cases of conjunctivitis cleared up with instillation of the 1 mg. per 1 ml. solution four times daily for five days. In the case of purulent arthritis, 10 ml. of the solution was injected into the joint daily for five days, with complete eradication of the organisms. In the case of chronic sinusitis daily irrigation of the sinus with a solution of 0.5 mg. per ml. for seven days resulted in eradication of the organisms and diminution of the discharge. No toxic symptoms were observed with the dosage schedules employed, and polymyxin B proved the most effective drug now available against *Pseudomonas aeruginosa* infections. 18 references. 2 figures. 2 tables.

A large number of pseudomonas infection have been successfully treated with the polymyxins. However, toxicity of both renal and nervous systems must be seriously considered for the physician who is not an investigator.—E.B.S.

oncology

80. *Radioactive Arsenic in the Treatment of Hodgkin's Disease and Mycosis Fungoides* (*L'arsenic radio-actif dans le traitement de la maladie de Hodgkin et du mycosis fungoide*). LUCIEN MALLET, GEORGES MARCHAL, AND GERARD DUHAMEL, Rome, Italy. Acta Haematologica *7*:27-38, January 1952.

The authors use As 76 as a solution of sulphurarseniate. This substance showed, in experiments on animals, a pronounced dermotropism. The radioactive solution was given orally under the necessary precautions.

In 2 cases of lymphogranulomatosis with cutaneous localization, the cutaneous manifestations and pruritus disappeared. One of these patients still shows a complete remission for 15 months.

Two patients in the terminal stage of mycosis fungoides showed, under the treatment with As 76, improvement of the skin changes and survived for four and six months, respectively.

With regard to its quick disintegration, As 76 must be applied without delay. The most important disadvantage of the oral method is the frequency of gastrointestinal side effects.

The marked dermotropic fixation of As 76 restricts the indications to the pruriginous and cutaneous forms of lymphogranulomatosis. 5 references. 6 figures.

The nitrogen mustards and triethylene-imino melamines are more reliable in these disorders.—E. B. S.

81. *The Effect of Cortisone in Hodgkin's Disease.* B. STRAUSS, A. S. JACOBSON, S. A. BERSON, T. C. BERNSTEIN, R. S. FADEM, AND R. S. YALOW. Am. J. Med. *12*:170, 1952.

Ten patients with advanced Hodgkin's disease were treated with 100-200 mg. doses of cortisone daily. Transient but significant improvement in the sedimentation rate, fever, malaise, anorexia, and weight loss developed in 7, fever subsided completely in 3, but only 1 patient showed regression of disseminated lesions.

When dosage was reduced to 300 mg. weekly, the symptoms and signs recurred. The addition of nitrogen mustard to the regimen produced no additive effect. Undesirable effects included gastro-intestinal bleeding and perforation, in addition to the development of mild symptoms of hyperadrenalism.

True remissions were not obtained with these agents, since relapse invariably occurred as soon as therapy was discontinued.

Effects of this regimen on potassium and iodine metabolism are described.

82. *The Serum Mucoproteins as an Aid in the Differentiations of Neoplastic from Primary Parenchymatous Liver Disease.* EZRA M. GREENSPAN, BERNARD TEPPER, LUTHER L. TERRY, Baltimore, Md., and EMANUEL B. SCHOENBACH, Brooklyn, N. Y. J. Lab. & Clin. Med. *39*:44-56, January 1952.

In an extension of previous studies, the serum mucoprotein (M) level, measured as biuret peptide, was estimated in 89 normal adult subjects. The normal limits of M varied from 40 to 70 mg. per cent in females (Mean, SD and S.E. = 54.3 ± 7.7 ± 1.2) and 48 to 75 mg. per cent in normal males (60.3 ± 7.4 ± 1.1).

A reduced mucoprotein (M) content of the serum was observed in 32 of 36 cases of acute homologous serum or infectious hepatitis and in 32 of 40 patients with portal cirrhosis, but in no case of hepatic metastases and in only one instance of obstructive or inflammatory biliary disease.

In the various categories of hepatomegaly and jaundice, the mean M levels were: (1) infectious hepatitis or homologous hepatitis, 38.6 mg. per cent, portal cirrhosis, 32.5 mg. per cent; (2) obstructive inflammatory or neoplastic disease of the biliary tract (acute or chronic cholecystitis, common duct stone, cholangitis, biliary cirrhosis, and biliary or pancreatic carcinoma), 82.9 mg. per cent; (3) hepatomegaly due to hepatic metastases, 116.1 mg. per cent.

The normal M level appears to represent an equilibrium between an intrahepatic factor (liver function) and such extrahepatic factors as cellular proliferation, necrosis, and inflammation. An M determination appears to be useful in the diagnosis of uncomplicated parenchymatous hepatic disease (hepatitis, portal cirrhosis) as in the medical versus surgical management of hepatomegaly and jaundice.

The relationship of serum mucoproteins to the alpha-globulins is discussed. 26 references. 5 figures.—*Author's abstract.*

respiratory diseases

83. *Acute Pulmonary Oedema, Endogenous and Exogenous Causes, with Therapy.* ELSTON L. BELKNAP, Milwaukee, Wis. Dis. of Chest *20*:630-41, December 1951.

Acute pulmonary edema of the massive type is likely to develop when the lungs are suddenly flooded with serous fluids. Such an incident may take place when the subject is in apparent health, or it may be brought on by some slight exertion or excitement. Occasionally, pulmonary edema may be the result of carelessness in treatment, as, for instance, in the administration of too rapid and massive an intravenous saline infusion or when a thoracentesis is performed too rapidly or too thoroughly. The etiologic theories, including the recent neurogenic theory, are reviewed.

It has been suggested that pulmonary edema may be attributable to leakage of the capillaries of the pulmonary epithelium lining the alveolar units, with abnormal transmission due to sustained increase in pulmonary capillary pressure or to tissue anoxia, which increases the permeability of the pulmonary capillaries. Exogenous causes include bronchial and pulmonary irritation by irritating or toxic gases. If the condition is due to inhalation of acid gases or irritating fumes, the best treatment consists of administration of oxygen under pressure, either with the intermittent positive pressure instrument or by use of the Barach oxygen mask. Following such therapy an improvement may be expected after one to three hours.

In some instances, further improvement may be obtained by serial application of tourniquets to the extremities or by venesection. Narcotics and sedatives, such as morphine, papaverin, chloretone, and phenobarbital are also helpful. Oxygen under slight positive pressure may also be useful. Inhalation of ethyl alcohol improved the survival time in animals.

A warning is issued that the use of carbon tetrachloride or other chlorinated solvents for cleaning purposes by housekeepers in the presence of high heat may lead to the formation of phosgene vapors that may cause fatal pulmonary edema. 19 references.

I would feel that the features of this paper most worthy of the attention of the internist are those concerning exogenous causes of acute pulmonary edema, their recognition and their management.—R. Mc L.

84. *Intravenous ACTH Therapy in the Treatment of Bronchial Asthma.* MAURICE S. SEGAL AND J. AARON HERSCHFUS, Boston, Mass. Dis. of Chest *20*:575-81, December 1951.

In previous reports, the authors have described their results in the treatment of severe bronchial asthma with intramuscular injections of ACTH. In the present

series of 10 cases, the ACTH was administered intravenously by continuous infusion. The total dose ranged from 10 mg. to 210 mg. over a period of one to nine days. Seven of these patients showed excellent remissions following this treatment, lasting up to six weeks. Others responded with partial remissions only, but there was no absolute therapeutic failure in the entire group. One patient, who had shown clinical resistance and eosinophile escape following intramuscular administration of ACTH, responded promptly to intravenous infusion. It is important to administer antibiotics, simultaneously, to patients who suffer from simultaneous bronchitic infection, in order to combat a lowered resistance to infection produced by the ACTH.

The authors conclude that intravenous ACTH constitutes a very effective treatment for severe bronchial asthma. Since the total dose is only 1/5 to 1/8 of that required for intramuscular injection of the drug, the intravenous method is less costly, and furthermore patients who show no response to intramuscular therapy may respond to the intravenous form of administration. There were no allergic reactions, but 2 patients had short febrile attacks following the medication, the cause of which could not be explained.

In some instances there occurred a rapid recurrence of the respiratory symptoms when the medication was discontinued. It is suggested that these results might be prevented by giving the patient large doses of oral or rectal aminophyllin and antibiotics when indicated. Possibly remissions might also be prolonged in this way.

In each case the patient is started on a continuous infusion of 6 per cent glucose in distilled water (3 liters per 24 hrs., 30 drops per minute flow) usually with 0.5 g. aminophyllin per liter of fluid. ACTH was added in the amount of 10 mg. per liter with a total dose of 30 mg. per 24 hours administered for one or more days. Then as symptoms subsided, the dose may be diminished to 15 or 10 mg. per 24 hours until a satisfactory result has been obtained.

Recently, this procedure was modified. After the second day of continuous infusion of ACTH, the latter is administered only in the first liter of fluid daily, while the infusion of glucose solution with or without aminophyllin is continued. The therapeutic effect is thus more rapid and is maintained throughout the 24 hours. 8 references. 1 table.

Although intravenous ACTH is an effective method of treating severe bronchial asthma, it should be employed as an emergency form of therapy to tide the patient over during a crisis. It should not replace the tried method of investigating and eliminating the underlying cause which can control attacks most effectively. Nor should it be used as a substitute for proper immunization. The routine administration of antibiotics is not without drawbacks. It should be given with great care. Many allergic patients, and especially asthmatics, may be sensitive to penicillin or sulfa drugs which can aggravate rather than ameliorate the asthma and in addition give rise to other allergic manifestations such as purpura, skin rashes, etc.—J.H.

85. *Diffuse Pulmonary Granulomatosis in Young Women Following Exposure to Beryllium Compounds in the Manufacture of Radio Tubes. Further Observations and Report of Nine Additional Cases.* PAUL SLAVIN, Newark, N. J. Am. Rev. Tuberc. *65*:142-58, February 1952.

Five cases of diffuse pulmonary granulomatosis, resulting from exposure to beryllium in the manufacture of radio tubes, were reported previously. Nine additional cases are presented in this paper.

Nine of the 14 patients had been working in a factory where beryllium had been used as an ingredient in the coating of filaments, hook wires, and cathodes, and also in the manufacture of automobile headlights. Several operations were accompanied by dispersion of beryllium dust through the surrounding air. No protection was provided against dust inhalation.

In the cathode-spray department, the air was filled with fine coating powder scattered by the spray guns.

Cleaning of the spray booths and of the racks and clips holding the cathodes and hook wires had been done at regular intervals by scraping off the spattered dry coating with a buffing wheel or hand files. The dust was then removed with a blower—a hose connected with compressed air.

The cutting and nicking of coated filaments by a drum-cutter caused scattering of coating dust through the surrounding air.

The assembling and mounting operations produced considerable dustiness, as some of the filament coating was chipped and scraped off by these procedures. Thousands of units were handled daily by an individual worker.

Three patients had been working in the spray department. Five patients had been engaged in assembling and mounting operations. Two patients had been working on cutting coated wires and filaments. The dust-producing operations in which the other 4 patients had been engaged remain unknown.

Single 24 hour samples of urine were examined, spectrographically, for beryllium in 5 cases. All of the examinations were negative.

The lung tissue was examined in 5 cases, and beryllium was found in each of them. No apparent relationship existed between the amounts of beryllium recovered and the extent of the pulmonary involvement.

The liver, kidneys, and spleen were examined in 2 cases. Beryllium was demonstrated in the liver and kidney of 1 case. In the other case, the three organs were examined jointly, and considerable beryllium was found.

Multiple bleb formation was observed on roentgenographic examination in all cases. In 1 case, giant multilocular blebs and numerous smaller ones simulated cystic lung disease. In 3 cases, large solitary blebs had the appearance of cavities. Rupture of blebs with a resulting pneumothorax occurred in 4 cases.

Chronic pulmonary beryllium granulomatosis is a grave, incurable disease. Due to lack of fever and pain, the patients in the present series sought medical advice when the ailment was far-advanced and their difficulty in breathing became disabling. Even then some of them continued to be exposed to beryllium, as there was a delay in recognizing the occupational nature of the illness. The expected survival

period from the beginning of disability varied, depending on the condition of the heart. The outlook was more favorable in patients with a stabilized granulomatous reaction and no *cor pulmonale*. 2 references. 14 figures.—*Author's abstract.*

cardiovascular diseases

86. *Pulmonary Function Studies in Polycythemia Vera: Results in Five Probable Cases.* WALTER NEWMAN, JAMES A. FELTMAN, AND BLANCHE DEVLIN. Am. J. Med. *11*:706-14, December 1951.

The authors report studies of pulmonary function in 5 cases of polycythemia, in all of which phlebotomy was done, the studies being made before and after this procedure. In all these cases, the maximum breathing capacity was increased after phlebotomy. In 1 case, there was diminution of ventilation and oxygen consumption, and hence decreased oxygen saturation during exercise; these values returned to normal after phlebotomy. In 2 cases there was a decrease in vital capacity and total capacity as well as in maximum breathing capacity, and in 1 of these cases a high diffusion gradient also was demonstrated. After phlebotomy, the lung volume and values for ventilation and gas exchange became normal in 1 of these cases, but in 1 the maximum breathing capacity, while increased by the phlebotomy, did not become entirely normal. These findings indicate that polycythemia, with its increase in the viscosity of the blood and in blood volume, causes decreases in the elasticity of the lungs and an increase in their viscous resistance, which result in diminution of the maximum breathing capacity and of the vital capacity, impairment of ventilation, and anoxia. This may involve damage to the respiratory center and, thus, establish "a vicious cycle." Since such changes are not always reversible, early adequate therapy is necessary in patients with polycythemia vera. 20 references. 2 tables. 1 figure.

87. *Primary Pulmonary Hypertension: Clinical and Hemodynamic Study.* DAVID T. DRESDALE, MARTIN SCHULTZ AND ROBERT J. MICHTOM, Brooklyn, N. Y. Am. J. Med. *11*:686-705, December 1951.

The authors report 3 cases of primary pulmonary hypertension and present a review of the literature. The primary symptoms of this syndrome are weakness and dyspnea on exertion, followed by signs of right heart failure, without clinical evidence of definite cardiac or pulmonary disease. Syncope and angina may occur on effort. The systemic blood pressure is normal, the lungs are clear on x-ray examination, and studies of pulmonary function in 2 of the 3 patients showed no evidence of intrinsic disease of the lungs. The pulmonic second sound is accentuated, but cardiac murmurs are either absent or variable. Electrocardiographic studies indicate right ventricular hypertrophy, and the x-ray examination shows enlargement of the right ventricle. The x-ray also shows bulging of the pulmonary artery segment, prominent hilar vessels, and either normal or diminished vascular markings in the lungs.

Catheterization of the right heart was done in the 3 cases reported. It showed marked elevation of pulmonary artery pressure, elevation of right ventricular systolic and diastolic pressure, diminished cardiac output, increase of arteriovenous oxygen differences, but normal oxygen saturation of the arterial blood. (None of these patients showed cyanosis except in the 1 fatal case in which cyanosis occurred before death.) All patients showed increased pulmonary resistance at rest. One of the 3 patients died in cardiovascular collapse in the hospital. Autopsy showed enlargement of the right atrium and ventricle with hypertrophy of the walls of the ventricle, left atrium and ventricle normal, no valvular disease; extensive vascular sclerosis in the lungs without intrinsic lung disease; the sclerotic lesions were most numerous in the small arteries where they developed over thrombotic lesions. These findings, as well as the physiologic studies in the 3 cases, indicate that the small pulmonary arteries are "the locus" of the increased pulmonary resistance. Priscoline, which is a sympatholytic agent, was effective in lowering the pulmonary artery blood pressure, indicating that "isolated overactivity" of the sympathetic nervous system is characteristic of these cases and suggesting the possible value of sympathectomy in the treatment of primary pulmonary hypertension—a subject requiring further investigation. 67 references. 3 tables. 18 figures.

88. *Blood Pressure Variations in the Two Arms.* MILTON J. RUEGER, Lancaster, Pa. Ann. Int. Med. *35*:1023-27, November 1951.

A series of 1,388 blood pressure readings on each arm of 755 consecutive patients was made during the course of regular office visits. A significant incidence of variation in both systolic and diastolic readings in the two arms was noted in patients with both normal and abnormal cardiovascular systems. This difference could be of vital importance to an individual when applying for life insurance, employment or military service and may mean acceptance or rejection in certain cases depending on which arm was used.

It is recommended that, at the first examination, the blood pressure be checked in both arms. 10 references. 1 table.—*Author's abstract.*

89. *Transient Inversion of T Waves after Paroxysmal Tachycardia.* RALPH M. MYERSON AND A. HENRY CLAGETT, Wilmington, Del. J. A. M. A. *148*: 193-96, Jan. 19, 1952.

An electrocardiographic syndrome consisting of transient inversion of T waves after paroxysms of tachycardia in normal hearts has been recognized for some time. The resemblance of these changes to those of serious organic heart disease makes the importance of their recognition and understanding obvious.

A review of the literature reveals 24 well documented cases of this syndrome, in addition to which the authors add 2 recently observed cases of their own.

Though most cases have been noted following paroxysmal ventricular tachycardia, this relationship may be more apparent than real. The duration of the tachycardia has no relationship to the magnitude or duration of the T wave changes.

No other consistent electrocardiographic variations such as ST segment changes

or development of Q waves occur. The pattern of T wave inversion may be "posterior," "anterior," or mixed.

The mechanism of post-tachycardial T wave inversion is unknown. Ischemic, anaphylactic, and autonomic theories have been proposed.

The authors present 2 cases of T wave inversion, following episodes of paroxysmal auricular tachycardia, in healthy young adult white males. 2 references. 3 figures. —*Author's abstract.*

90. *Diffuse Arteritis of Unknown Origin Accompanied by Eosinophilia.* K. W. WALTON, Birmingham, England and D. W. ASHBY, London, England. Brit. M. J. *4743*:1310-15, Dec. 1, 1951.

Morphologically, similar changes have been described as affecting the arteries in a number of clinically different conditions. These arterial changes may be acute or chronic but are all of an inflammatory granulomatous character. The inflammatory exudate often contains eosinophils, and there may be an accompanying peripheral eosinophilia. The latter may be so intense as to lead to the misdiagnosis of eosinophilic leukemia.

The histologic similarity between the vascular and connective tissue lesions of the various collagen diseases, such as polyarteritis nodosa, lupus erythematosus disseminatus, generalized scleroderma, dermatomyositis, rheumatic polyarteritis, and other less well defined entities, has occasioned speculation about whether the lesions have a common etiologic origin in being hypersensitive or allergic reactions.

A case is reported which shows a diffuse arteritis and presents a clinical picture having features in common with polyarteritis nodosa, temporal arteritis, eosinophilic leukemia, and with one variety of sensitization reaction to drugs. The case did not correspond entirely with any one of these and, though it was suspected on general grounds to be allergic in origin, no proof of this was obtained.

The patient was a male, aged 56, who developed successively: (1) gastroenteritis; (2) a skin rash starting as a diffuse erythema and progressing to generalized exfoliation; (3) Raynaud's symptom complex, leading to gangrene of the fingers; (4) transient visual disturbances; (5) enlargement of spleen and lymph nodes; (6) pyrexia and leukocytosis with marked eosinophilia; (7) thrombosis of temporal and radial arteries.

Biopsies from various sites showed evidence of widespread inflammatory arteritis with eosinophilic infiltration of the tissues and viscera.

The patient made a remarkable and unexpected recovery without any specific therapy. The relationship of this case to various other conditions, showing similar histologic changes and of supposedly allergic origin, is discussed. 34 references. 8 figures.—*Author's abstract.*

91. *Surgery of Acquired Valvular Disease.* ROBERT W. WYLIE, New York, N. Y. Bull. New York Acad. Med. *28*:106-17, February 1952.

A short review of the historical background of the present surgical approach to mitral stenosis is followed by a description of the pertinent physiologic and anatomic

basis for the direct operation on the valve. A brief outline of the technic of surgery is followed by the indications and selection of patients. An estimate of the present status of the operative treatment is given from the point of view of mortality and results to date. 22 references.—*Author's abstract.*

92. *The Ballistocardiogram in Coronary Artery Disease.* ROBERT C. TAYMOR, LEON PORDY, KENNETH CHESKY, MARVIN MOSER AND ARTHUR M. MASTER, New York, N. Y. J. A. M. A. *148*:419-23, Feb. 9, 1952.

Employing the simplified direct photoelectric type of ballistocardiographic instrument, the ballistocardiogram was analyzed in 195 subjects with and without coronary artery disease. The results were correlated with those of the "two step" exercise electrocardiogram. The ballistocardiogram was recorded while the subject was at rest and after standard exercise. Only when the recording was normal before and after exercise was the ballistocardiogram considered to be normal. Ninety-five per cent of the patients with other evidence of coronary artery disease had abnormal ballistocardiograms, either at rest or after exercise. Fifteen per cent of the patients with no evidence of coronary artery disease, including electrocardiographic studies, showed abnormal ballistocardiograms. This occurred twice as frequently in patients 50 years of age or older as in patients under 50 years of age.

The authors emphasize that, since the ballistocardiogram represents mechanical cardiac function and the electrocardiogram is a reflection of the electromotive field of the heart, no point to point correlation between the two should be expected. Either the ballistocardiogram or the electrocardiogram may be the first to demonstrate abnormality early in the natural history of coronary artery disease. In some cases of coronary artery disease, cardiac ejection force, and thus the ballistocardiogram, may be normal at rest and abnormal only after exercise. Therefore, the ballistocardiogram should be recorded after exercise when the resting record is normal.

Since most "normal" patients with abnormal ballistocardiograms were in the older age group, it was felt that this may be associated with other "physiologic" aging processes and have little prognostic significance. In the younger age group, however, the presence of an abnormal ballistocardiogram may be of importance in regard to abnormal cardiac function. Follow-up studies on this and other groups will be necessary to ascertain the full significance of these findings.

The ballistocardiogram will serve as a useful adjunct in the diagnostic examination of patients suspected to have coronary artery disease.—16 references. 3 figures. 4 tables.—*Author's abstract.*

93. *Roentgen Aspects of Pulmonary Arteriovenous Fistula.* WILLIAM B. SEAMAN AND ALFRED GOLDMAN, St. Louis, Mo. A. M. A. Arch. Int. Med. *89*:70-81, January 1952.

Roentgenographic studies of 8 cases of pulmonary arteriovenous fistulas are reported; clinical studies of 4 of these cases have been previously reported. The ages of these patients varied from 22 to 79 years; the oldest patient was in general

good health and was referred for study because roentgenologic examination for virus pneumonia had shown a pulmonary mass, the nature of which was not determined. With the usual chest roentgenogram, the diagnosis of pulmonary arteriovenous fistula can be made if there are tortuous and bandlike opacities, communicating with the hilum and also with a lobulated soft-tissue tumor in the parenchyma. If the fistulas are small, the appearance of the opacities may not be characteristic and may resemble other pulmonary lesions.

In establishing the diagnosis, it is most important to demonstrate the relation of the mass to the blood vessels. In the fluoroscopic study, the Müller test may be used; it increases the negative intrathoracic pressure, which results in a distention of the fistula with blood. This test is not always positive and was not used in all the 8 cases reported, but was positive in 2 of them. The authors are of the opinion that this procedure should be used when pulmonary arteriovenous fistula is suspected but not definitely demonstrated by the usual roentgenologic methods. In some cases, the pulsatile nature of the mass may be demonstrated both by fluoroscopy and by roentgen kymography; pulsations were demonstrated by both methods in 2 of the authors' cases. Laminography is a valuable method of demonstrating the vascular relations of the pulmonary shadow and, employed with the usual chest roentgenograms, is usually sufficient to establish the diagnosis of pulmonary arteriovenous fistula. Angiography has been used in some cases, but involves danger of sudden death, especially in patients with hypertension or cardiac failure. The authors are of the opinion that it should be employed if surgical treatment is contemplated, especially as it is of value in demonstrating multiple lesions not otherwise discovered. 20 references. 1 table. 10 figures.

94. *The Response of Patients with Congestive Heart Failure to a Rapid Elevation in Atmospheric Temperature and Humidity.* G. S. BERENSON AND G. E. BURCH, New Orleans, La. Am. J. M. Sc. 223:45-53, January 1952.

Observations were made to investigate the intolerance of patients with cardiac disease and congestive heart failure to stress of a hot and humid environment.

Thirteen patients in various stages of congestive failure were studied by clinical methods, including measurements of blood pressure, cardiac and respiratory rates, and rectal and skin temperatures. Comparisons were made with 13 control subjects. In three experiments, one control subject and one patient with congestive failure were studied simultaneously. Following observations in comfortable atmospheric conditions, response to a hot and humid atmosphere (40° ± 2°C., 85 per cent RH) for periods of 40 to 114 minutes was noted.

The heated surroundings precipitated acute attacks of "left ventricular failure" (cardiac asthma), characterized by severe dyspnea, orthopnea, and pulmonary rales, associated with apprehension in 5 subjects with cardiac disease. Gallop rhythm developed or was accentuated in 9 patients. Ability to withstand stress of a hot, humid environment was definitely less in subjects with congestive heart failure. This group exhibited primary cardiovascular and pulmonary intolerance, whereas many central nervous system disturbances developed in the controls;

they were able to endure sufficiently prolonged exposures to the environment. The cardiovascular reactions in control subjects tended to be more uniform and were characterized especially by elevation of pulse pressure.

These experiments indicate the intolerance of patients with certain types of cardiac disease to a hot and humid atmosphere and also suggest need for control of environmental atmosphere during therapy. 17 references. 3 figures. 1 table.—*Author's abstract.*

95. *False Positive Reaction to the Piperoxan Hydrochloride Test for Pheochromocytoma.* ALFRED SOFFER, Rochester, N. Y. J. A. M. A. *148*:538-40, Feb. 16, 1952.

Pheochromocytomata are frequently associated with sustained hypertension and this clinical state may simulate that of essential or malignant hypertension. In these cases the piperoxan hydrochloride test has been proved to be of continuous diagnostic value. Goldenberg and Aranow have stated that in the several thousand tests performed in this country and in Great Britain no proven false positive results have been reported. Since their report, a false positive reaction to the piperoxan test confirmed by autopsy has occurred.

A 57 year old housewife was first treated for hypertensive encephalopathy in 1947. Her clinical state deteriorated progressively, and in November 1950 the patient was hospitalized in uremia and in a state of semistupor. A piperoxan hydrochloride test performed at this time produced a blood pressure drop that was consistent with the diagnosis of pheochromocytoma. The patient expired two days later, and a postmortem examination revealed the absence of a chromaffin tissue tumor. The final pathologic diagnoses were chronic pyelonephritis and marked arteriolar nephrosclerosis, generalized arteriosclerosis and arteriolar sclerosis, cardiac hypertrophy and dilatation, and cerebral edema.

Wilkins and associates have reported that 8 per cent of their patients responded to the piperoxan hydrochloride test with alarmingly severe reactions, primarily pressor in nature. Goldenberg and Aranow have noted that in a large number of piperoxan hydrochloride tests there have been no instances of persistent damage. It is concluded that the transient blood pressure fall following the piperoxan hydrochloride test in this patient was not directly related to the outcome. 13 references. 3 figures.—*Author's abstract.*

gastrointestinal diseases

96. *Multiple Liver Abscesses Complicating Non-Specific Chronic Ulcerative Colitis: Report of a Case.* JEROME V. TREUSCH, Los Angeles, Calif. Gastroenterology *20*:166-73, January 1952.

Multiple liver abscesses are a very rare and interesting complication in nonspecific ulcerative colitis. This is in sharp contrast to the situation in amebic colitis. A case in a 20 year old female patient is reported in detail of nonspecific

chronic ulcerative colitis complicated terminally with multiple liver abscesses, in which the diagnosis was presumptively made pre-mortem. The autopsy findings with illustrations are included. The possible explanations for the rarity of this complication in a disease where it might be expected to occur frequently are reviewed, and include: (1) the strong detoxifying and bactericidal power of the liver and (2) the chronicity of the disease which gives the body ample opportunity to throw up local barriers and to produce systemic immunity. These factors were counterbalanced possibly in the case reported by lowered resistance associated with poor germ plasm evidenced by the presence of multiple congenital anomalies. 7 references. 6 figures.—*Author's abstract.*

97. *Unfavorable Course of Gastric Ulcer during Administration of ACTH and Cortisone.* JOSEPH B. KIRSNER, ARTHUR P. KLOTZ AND WALTER L. PALMER, Chicago, Ill. Gastroenterology *20*:27-29, January 1952.

Ulcer symptoms recurred shortly after the administration of ACTH in two patients with gastric ulcer; in one a previously demonstrated crater increased in size; in the other case the ulcer recurred and perforated after 21 days of ACTH. In a third patient, a huge gastric ulcer developed within 10 days after the administration of cortisone. An increased output of acid gastric juice was demonstrated in the two in whom gastric secretion increased. 9 references.—*Author's abstract.*

98. *Transabdominal Cholangiography.* B. FRANKLIN CARTER AND GEORGE M. SAYPOL, New York, N. Y. J. A. M. A. *148*:253-55, Jan. 26, 1952.

Despite the value of liver function tests to differentiate hepatocellular from extrahepatic obstructive jaundice, there remains the occasional case in which one cannot be certain of the diagnosis. Cholangiography, without operation, by revealing obstruction and dilatation of bile ducts can be of great assistance in a questionable case. To date, it has been used only in well selected cases, i.e., where the liver can be felt abdominally in a patient whose condition is so poor that abdominal exploration is hazardous.

The procedure is performed in the operating room. The usual preparations for immediate cholangiography are made. One per cent procaine locally or intravenous sodium pentothal is employed. A No. 17 spinal needle without obturator is then inserted through the abdominal wall into the left lobe of the liver in the direction of the bile ducts. When blood is obtained, the needle is inserted further or withdrawn slightly as the hepatic vessels are in close apposition to the hepatic ducts. After bile is flowing from the needle, it is aspirated and then 15 to 25 cc. of 35 per cent diodrast is injected. Films are taken by the usual technic. The needle is fixed and strapped firmly to the skin surface to allow bile to drain externally.

Photographs illustrate the technic. A case history is presented in which transabdominal cholangiography revealed an obstruction of the common hepatic duct. The patient died three days after the procedure from massive hemorrhage in the gastrointestinal tract, the result of portal hypertension. Autopsy revealed adenocarcinoma of the common hepatic duct. 8 figures.—*Author's abstract.*

99. *Antibacterial Action of Oral Aureomycin on the Contents of the Colon of Man.* WILLIAM I. METZGER, LOUIS T. WRIGHT, ROBERT F. MORTON, JAMES C. DILORENZO AND MILTON MARMELL, New York, N. Y. Antibiotics and Chemotherapy *2*:91-102, February 1952.

The effect of oral aureomycin on the intestinal flora of 15 adult hospital patients, who were normal from a gastrointestinal viewpoint, was studied in detail. The average dosage of aureomycin was 1.0 Gm. three times daily for 3 to 4 days. In addition, each patient received daily cathartics and enemas and a low residue diet. Pour plate counts were made of the principal intestinal organisms, including aerobes and anaerobes. The pour plate technic, when compared with the less quantitative streak plate method, proved to be considerably more reliable.

The results showed that coliform organisms (*E. coli, A. aerogenes* and intermediates) generally were markedly reduced in numbers but reappeared soon after the drug was stopped. The same was true for sporeforming organisms (aerobic and anaerobic) and for nonsporeforming anaerobes (*Bacteroides*). In 11 of the 15 cases, *Proteus* organisms multiplied noticeably following these reductions. On the other hand, medication stimulated the proliferation of gram positive cocci (streptococci and staphylococci) and of yeasts (*Monilia*) in many of the patients. When Paraben (methyl and propyl p-hydroxybenzoic acids) was contained in the aureomycin capsule (as a preservative), the yeast counts were reduced significantly. *In vitro* sensitivity studies on many of these organisms showed them to be relatively insensitive to aureomycin, as well as to terramycin, chloramphenicol and streptomycin. However, assays of stool contents showed a high concentration of aureomycin. It is postulated that (1) this aureomycin may be chemically bound in the bowel in an insoluble complex, or (2) the bacteria may be protected from the antibiotic by a coating with certain intestinal contents (fats, etc.).

The following conclusions were drawn:

1. The intestinal tract of man is by no means sterilized by the use of oral aureomycin, although this drug probably is as beneficial as any other single, nontoxic agent known at the present time.

2. Methodology is of prime importance in a study of this type, where the results are dependent almost entirely upon the bacteriologic data.

3. Until more is known regarding infective doses and pathogenesis of intestinal organisms in the peritoneum, it is unwise to label certain organisms as pathogenic and others as saprophytic for purposes of evaluating the benefit derived from any therapeutic agent for bowel sterilization. 21 references. 1 table.—*Author's abstract.*

100. *The Roentgen Diagnosis of Prolapse of the Gastric Mucosa into the Duodenum.* MAURICE FELDMAN AND PHILIP MYERS, Baltimore, Md. Gastroenterology *20*:90-99, January 1952.

The purpose of the authors' paper is fivefold: (1) to establish the incidence of prolapse; (2) to determine the incidence of the association of duodenal ulcer and gastritis; (3) to discuss the chief etiologic factors; (4) to discuss the clinical aspects; and (5) to present the roentgenologic criteria.

In 371 consecutive roentgen gastrointestinal studies, a prolapse of the gastric mucosa was observed in 52 cases, an incidence of 14 per cent. The high incidence is attributed to the fact that this group consisted of patients with gastrointestinal complaints. The chief etiologic factors are redundant mucosa, gastritis, and increased gastric peristalsis.

Of the 52 cases of prolapse of the gastric mucosa, an associated duodenal ulcer occurred in 20 or 38.5 per cent, and a gastritis in 24 or 46 per cent.

The varying degrees of prolapse are discussed. The degree of prolapse depends upon several factors: (1) amount of redundant gastric mucosa; (2) extent of the prolapse; and (3) height of peristaltic activity. The degree of prolapse seems to vary in the same patient and at different intervals.

The characteristic roentgen picture of prolapse of the gastric mucosa into the duodenal bulb is presented with illustrations. 16 references. 3 figures.—*Author's abstract.*

101. *Gastric Secretory Response to 3-Beta Aminoethyl Pyrazole in Man.* JOSEPH B. KIRSNER, ERWIN LEVIN, WALTER L. PALMER AND HAROLD FORD, Chicago, Ill. Gastroenterology *20*:138-42, January 1952.

The gastric secretory response to 3-beta aminoethyl pyrazole, an analog of histamine, was studied in 50 individuals (22 with no organic disease, 24 with peptic ulcer and 4 with miscellaneous lesions). The secretory response to the analog approximated that elicited by histamine. The tendency to side effects was far less than with histamine. 2 references. 4 figures. 1 table.—*Author's abstract.*

102. *Complications of Gastrointestinal Diverticula Demonstrated by X-ray.* ERNEST A. MENDELSOHN, Fort Smith, Ark. Gastroenterology *20*:105-118, January 1952.

The radiologist often considers a diverticulum a harmless finding and attributes little clinical importance to its presence. Nevertheless, complications of certain diverticula of the gastrointestinal tract are sometimes found at the operating table, and then constitute indications for surgery.

A group of 8 cases of gastrointestinal diverticula is reported, in which complications arising within the diverticula were the cause of major gastrointestinal symptoms. The diverticula and the pathology associated with them were successfully demonstrated by x-ray examination. 27 references. 8 figures.—*Author's abstract.*

103. *Endemic Infectious Hepatitis in an Infants' Orphanage: Epidemiologic Studies in Student Nurses.* RICHARD B. CAPPS AND ALFRED M. BENNETT, Chicago, Ill. and JOSEPH STOKES, JR., Philadelphia, Pa. Arch. Int. Med. *89*:6-23, January 1952.

In a study of the epidemiology of infectious hepatitis among student nurses in an orphanage, caring for children less than three years old, it was demonstrated that some of the children had infectious hepatitis and that these children infected the

student nurses by person-to-person contact. The presence of infectious hepatitis in 26 children was established by clinical and laboratory studies and by the infection of volunteers with material from the feces of 2 children with the disease. All but one of these children, however, were free from jaundice or hyperbilirubinemia, thus indicating the importance of unrecognized, nonjaundiced cases in the spread of infectious hepatitis. For several months during the period of this study, gamma globulin was given to student nurses on admission to training; during this period only 1 case of infectious hepatitis developed among the student nurses, and in this case gamma globulin was given too late. The establishment of aseptic nursing technic throughout the orphanage resulted in preventing further spread of infection and terminated the outbreak of the disease among the nurses. 39 references. 6 tables. 8 figures.

This is an excellent study and presentation. The importance of unapparent infection in the transmission of infectious hepatitis is evident. The use of gamma globulin as a prophylactic measure has not been established with the data presented.—E. B. S.

104. *Incidence of Hepatitis among Narcotic Addicts in the Harlem Hospital, New York.* ALEXANDER ALTSCHUL, PEARL D. FOSTER, SAMUEL S. PALEY AND LEONA TURNER, New York, N. Y. Arch. Int. Med. *89*:24-31, January 1952.

In 1950, 5 patients were admitted to Harlem Hospital with symptoms of hepatitis, who were found to be drug addicts. Definite jaundice was present in 4 of these 5 patients, and 1 without jaundice showed other evidence of hepatitis. All of these patients used heroin, and 4 administered the drug intravenously; the fifth patient employed hypodermic injections. In these cases the hepatitis was of the infectious (virus) type, and was undoubtedly due to lack of effective sterilization of the syringes and needles or of the drug employed. Inquiries among physicians in private practice in the area served by the hospital showed that they had noted a sudden increase in jaundice among narcotic addicts during the summer and fall of 1950, indicating transmission of the infection by the same means as in the patients admitted to the hospital. 13 references. 2 tables.

105. *Use of Corticotropin and Cortisone in Acute Homologous Serum Hepatitis.* HAROLD RIFKIN, LEON J. MARKS, DAVID J. HAMMERMAN, MORTIMER J. BLUMENTHAL, ALTER WEISS AND BERTHOLD WEINGARTEN, New York, N. Y. Arch. Int. Med. *89*:32-40, January 1952.

In 4 cases of acute homologous serum hepatitis, corticotropin or cortisone was employed, when the patients failed to improve although taking a fairly satisfactory diet supplemented by vitamins and liver extract given parenterally. In all these cases the administration of corticotropin or cortisone resulted in prompt clinical improvement and increased appetite. In 2 of the 4 cases a relapse occurred after the steroid treatment was discontinued, but this also responded promptly to another course of treatment. Although corticótropin and cortisone undoubtedly halt the rapid progress of acute homologous serum hepatitis, they do not necessarily alter

the basic mechanism of the disease. In 1 of the cases reported the condition had advanced to a typical phase of chronic hepatitis. The exact mode of action of cortisone and corticotropin in acute hepatitis has not been determined. 13 references. 3 figures.

Studies previously reported on the use of ACTH and cortisone in the treatment of infectious hepatitis have not indicated that more is accomplished than the nonspecific increase in appetite and well being. The complications encountered and the overall effect on the course of the disease were of such nature as to lend little support to the therapeutic value of ACTH or cortisone.—E. B. S.

106. *The Effect of BAL (2,3-Dimercaptopropanol) on Hepatolenticular Degeneration (Wilson's Disease).* D. DENNY-BROWNE AND HUNTINGTON PORTER, Boston, Mass. New England J. Med. 245:917-25, Dec. 13, 1951.

Hepatolenticular degeneration (Wilson's disease) is a chronic degenerative disease of the nervous system associated with a visceral disorder—cirrhosis of the liver, in some cases with mild recurrent hepatitis. A number of investigators have found that a marked increase in the copper content of both the liver and the brain is characteristic of Wilson's disease. In 1948, Mandelbrote and associates, while studying the mobilization of copper by BAL in multiple sclerosis, found that one of their control patients who had Wilson's disease also showed a marked increase in the urinary output of copper after administration of BAL. The authors tested the effect of BAL on the urinary excretion of copper in 2 patients with Wilson's disease and found that there was a sevenfold increase in the urinary excretion of copper following the administration of BAL but no change in the urinary excretion of amino acid, which is abnormally high in Wilson's disease. As both these patients showed definite clinical improvement after the administration of BAL, 3 other patients with Wilson's disease were also treated with BAL. All of the 5 patients showed symptoms of the "pseudosclerotic" type of the disease; the duration of the disease before the patients needed assistance in eating, dressing and walking varied from 4 to 13 years. Two patients were unable to move without assistance at the time that BAL was instituted. BAL was given at first in 4 daily injections; a dosage up to 2.5 mg. per Kg. body weight caused no severe toxic symptoms, but nausea and sometimes vomiting occurred. Recently BAL has been given in 2 daily injections for 10 to 12 days. Employing this method of administration the urinary excretion of copper has remained high. It is important that BAL be administered by intramuscular injection.

All but one of the 5 patients treated are now able to care for themselves; in the one patient who has not shown the same degree of improvement, there was a severe degree of both physical and intellectual deterioration before BAL was used. To maintain improvement, all patients require repeated courses of BAL (maintenance therapy) as symptoms of relapse begin to appear in 3 to 6 months after each treatment. A course of treatment with 2 daily injections of 1 to 1.5 cc. of BAL for 10 days every second month has been found to be a satisfactory method of maintenance therapy. While these studies indicate a direct relationship between the

neurologic symptoms of Wilson's disease and the accumulation of copper in the liver and brain, they do not solve the problem of the pathogenesis of the disease. 37 references. 1 table. 2 figures.

genitourinary diseases

107. *Studies of Fluid, Electrolyte and Nitrogen Balance in Acute Renal Insufficiency.* LLOYD T. ISERI, THOMAS M. BATCHELOR, ALBERT J. BOYLE AND GORDON B. MYERS, Detroit, Mich. Arch. Int. Med. *89*:188-215, February 1952.

In the 5 cases of acute renal insufficiency reported, 4 showed the typical syndrome of lower nephron nephrosis, and 1, caused by sulfonamide intoxication, showed evidence of a primary glomerular lesion. Of the 4 cases of lower nephron nephrosis, the cause of the renal insufficiency was diabetic coma in 1 case, and severe hemorrhage in the other 3 cases; the hemorrhage was associated with toxemia of pregnancy in 1 case, and in another a transfusion reaction was probably a factor. During the phase of oliguria in the cases of lower nephron nephrosis, there was a diminution of both the sodium and the chloride of the blood plasma. Two of these patients showed excessive water retention on a fluid intake of 3 liters daily in addition to the electrolyte disturbance, which resulted in water intoxication and pulmonary edema in 1 case and peripheral edema in the other. One of these patients showed an excess of plasma potassium during the period of oliguria; in the other patients in this group a low protein, high dextrose regimen prevented the development of hyperkalemia.

In all the cases of lower nephron nephrosis there was an increase in the nonprotein nitrogen of the blood during the period of oliguria. In the diuretic phase, there was considerable variation in the sodium and chloride of the plasma. There was a tendency to further reduction in the concentration of these electrolytes at the onset of diuresis, but the administration of isotonic saline solution to correct this must be carefully controlled, by determining both the plasma and the urinary concentrations of sodium and chloride. If laboratory facilities are not available for such determinations, the authors suggest that sufficient sodium and chloride should be given with water to make an approximately half isotonic solution. Three patients showed a potassium deficiency during the period of diuresis, which required administration of 100 mEq. potassium or more for correction. There was no immediate fall in the blood nonprotein nitrogen at the onset of diuresis, but a reduction occurred later with increased nitrogen elimination due to the increase in the volume of urine and/or an increase in the urinary concentration of nitrogen.

In the 1 case in which the renal lesion was primarily glomerular, there was an increased nonprotein nitrogen concentration in the blood, which gradually diminished after the urinary output was increased under treatment; this decrease did not begin, however, until after the sixth day of diuresis. The significant electrolyte disturbances characteristic of the cases of lower nephron nephrosis were not observed in this case, although there was a fall in the plasma sodium and chloride, during the first six days of diuresis. 24 references. 7 tables. 2 figures.

108. *Practical Control of Fluid and Electrolyte Balance in Carbon Tetrachloride Poisoning.* ROBERT C. PARTENHEIMER AND DAVID S. CITRON, Boston, Mass. Arch. Int. Med. *89*:216-33, February 1952.

In the past eighteen months 7 cases of carbon tetrachloride poisoning have been observed at the U. S. Public Health Service Hospital of Boston, in which the syndrome of lower nephron nephrosis developed. In the authors' experience at this Hospital, carbon tetrachloride poisoning is the most frequent cause of this syndrome and they are of the opinion that a history of exposure to carbon tetrachloride should be sought for in cases of acute urinary suppression without definite known cause. In the early stages of carbon tetrachloride poisoning, the chief symptoms are abdominal pain and tenderness, nausea and vomiting—symptoms that suggest the possibility of an acute surgical condition. Two of the patients in this series were first sent to a surgical ward.

As in other cases of lower nephron nephrosis, there was a period of anuria followed by diuresis. During the anuric stage, sodium and fluid intake should be restricted; carbohydrates should be given during this phase, either intravenously in the form of dextrose solution, or rice and karo® corn syrup can be given if the patient can take food by mouth. Carbohydrate is of value because it reduces the amount of tissue breakdown, thus reducing the liberation of both urea and potassium; vitamins A, B, K and C should also be given daily. Excessive potassium blood levels are also observed in the stage of anuria. This may be treated by gastric lavage with distilled water, as was done in 2 of the cases reported, or by the administration of cation-exchange resins. In the stage of diuresis, however, there is a definite potassium deficiency as well as a deficiency of sodium and chloride. Daily electrocardiograms are of value because of definite changes indicative of either hyperkalemia or hypokalemia. Saline solution may be indicated in this stage but under careful control by daily serum chloride determinations. If indicated by the electrocardiographic findings showing definite hypokalemia, potassium chloride and orange juice should be given by mouth, unless vomiting makes this impossible, in which case potassium chloride should be given parenterally. If increased excretion of calcium during the diuretic phase results in calcium deficiency, calcium should be given orally or parenterally before potassium is given, if there is also a hypokalemia. All but 1 of the 7 patients in this series recovered. 20 references. 3 tables. 6 figures.

musculoskeletal diseases

109. *The Clinical Effects of Delta 5 Pregnenolone in Rheumatoid Arthritis.* ALTON B. HIGGINS, RICHARD E. JONES AND THOMAS W. D. SMITH, Washington, D. C. U. S. Armed Forces Med. J. 29:1717-22, November 1951.

The method of the controlled placebo experiment has become essential to the study of a therapeutic material of the type discussed here. The remissions observed with cortisone were not present when delta 5 pregnenolone, a synthetic com-

pound with a structural formula related to that of cortisone, was used in the treatment of rheumatoid arthritis. Metabolically, none of the effects observed with cortisone occurred after the use of pregnenolone. 8 references. 4 tables.—*Author's abstract.*

110. *New Developments in the Use of Cortisone in Rheumatoid Arthritis.* PAUL J. BILKA, Minneapolis, Minn. Minnesota Med. *34*:1088-91, November 1951.

The clinical experience with the use of cortisone in the treatment of 50 patients with rheumatoid arthritis is presented. All patients obtained some subjective and objective improvement with the majority obtaining rather marked relief. However, this improvement was promptly lost in the majority of patients on cessation of cortisone. Several methods of administering cortisone were tried in an attempt to increase the remission or residual improvement rate. Preliminary data from 12 patients given combined cortisone and gold indicate a residual improvement rate comparable to that from gold alone. Experiences with the development of hypercortisonism and the complications of cortisone therapy are recorded. Long term maintenance cortisone administration appears to be a practical form of management but adequate information is not yet available regarding possible additional harmful effects. Cortisone used in association with physical medicine and orthopedic surgery offers considerable aid in the rehabilitation of the severe arthritic. 2 references. 2 figures. 5 tables.—*Author's abstract.*

111. *Cortisone and ACTH in Treatment of Ankylosing Spondylitis.* F. DUDLEY HART, London, England. Brit. M. J. *4751*:188-90, Jan. 26, 1952.

In Great Britain most workers still consider ankylosing spondylitis as something distinct from rheumatoid arthritis. In this they differ from most workers in the United States.

Hart et al (1949) have argued that until something is known of the etiology of both diseases, there is little to be gained by merging two unknowns and stating they are one, when the points of clinical, radiological and therapeutic differences are so many.

Assessment of improvement was by: (1) spinal flexion and extension as measured by an angled "spondylometer," which, extending from sacrum to cervical vertebrae, eliminates hip movements; (2) simple forward bending which includes hip movement, measurement being taken from fingertips to the floor at the tip of the big toes; (3) chest expansion, measured in inches at nipple level; (4) vital capacity estimations; and (5) subjective assessment of pain and stiffness by the patient himself, complete normality being taken as zero. Photographic contrast has not been sensitive enough to record small differences, and sedimentation rates have been so erratic as to be entirely unreliable.

There was, therefore, unlike the ring measurement of finger-swelling in rheumatoid arthritis, no absolutely objective measurement in ankylosing spondylitis which cannot be influenced by pain relief or psychologic factors.

Ankylosing spondylitis is a disease which lasts for many years or for the rest of

a patient's lifetime; one can never be sure that even a prolonged remission of many years will be a permanent one. ACTH or cortisone therapy can, therefore, only be given over a relatively short period in the life history of the disease.

Even if supplies of ACTH and cortisone were completely unrestricted it is very arguable if they would be more than short-term weapons in the treatment of ankylosing spondylitis, as they are, in no sense, curative. Exercises, postural drill and treatment of postural defects remain as necessary as before, and deep x-ray therapy, because of the prolonged improvement which follows it, still holds its place in therapy. 3 references. 3 tables.—*Author's abstract.*

neurology and psychiatry

112. *Variability of Signs in Multiple Sclerosis.* IRVING C. SHERMAN, Lancaster, Pa. Ann. Int. Med. *35*:1329-35, December 1951.

A group of 42 patients with multiple sclerosis were examined to analyze the variability of the manifestations in this disease. There were six patients with persistent paraplegia. Thirteen were so disabled as to walk only with great help. The remaining 23 were sufficiently ambulatory to keep up with their work. Eighteen items of the neurologic examination were selected and each was graded as to the degree of disability. The course of each patient's illness could be charted at successive examinations. A study was made of the variability of pathologic changes for each group.

A group of 42 patients was observed in Michael Reese Hospital for three weeks and the clinical status at discharge was compared with that on admission. Out of 466 pathologic findings, there were 69 instances of improvement scattered among 32 patients and at the same time 39 signs of regression among 30 patients. Twenty-three patients were followed after discharge for from three to thirty months. Comparison of the initial and final examinations revealed that out of 265 pathologic signs, there were 66 instances of improvement scattered among 21 patients and 58 signs of regression in 19 patients.

The most variable signs were cerebellar, clonus, Hoffman's sign, nystagmus and bladder disorders. All other signs fluctuated at one time or another except for speech. This was in addition to several acute neurologic episodes of disability.

This study reiterates the episodic and recurrent nature of some cases of multiple sclerosis. Furthermore, it calls attention to the fact that there may be variability in the objective signs without the appearance of any gross episodic disorders. 1 reference. 4 tables.—*Author's abstract.*

113. *The Alleged Sedative Effect of Thonzylamine Hydrochloride (Neohetramine).* CARNEY LANDIS AND JOSEPH ZUBIN, New York, N. Y. J. Lab. & Clin. Med. *38*:873-80, December 1951.

The purpose of this study was to determine whether thonzylamine hydrochloride taken in the usual clinical doses produces sedation in performance and in feeling

tone. The following performance tests were utilized: choice speed test, continuous problem experiment, cancellation, tapping speed, tapping endurance, critical flicker fusion (espiscotister, and critical flicker fusion) and strobotac. The reliability of these tests was found to vary between .75 and .86. The sensitivity of the tests to drug influences was determined by utilizing phenobarbital as a depressant and contrasting its effect with a neutral placebo. The effect of phenobarbital was to depress the level of performance significantly below the placebo level. When these tests were applied to subjects who were given thonzylamine hydrochloride it was found that their performance was not affected adversely on any of the tests, although they reported that they felt different during the period of ingestion. It may be concluded that thonzylamine hydrochloride does not give rise to true sedation. 14 references. 3 tables.—*Author's abstract.*

For Reference Only

114. *Psychological Problems in Physical Rehabilitation: A Review.* ROBERT H. BARNES, Denver, Colo. Am. J. M. Sc. *223*:106-12, January 1952.

For Reference Only

115. *Licensure or Certification of Clinical Psychologists.* FRANCIS J. GERTY, J. W. HOLLOWAY, JR. AND R. P. MACKAY, Chicago, Ill. J. A. M. A. *148*:271-73, Jan. 26, 1952.

hematopoietic diseases

116. *Late Lymphatic Leukemia Complicating Hypersplenic Syndrome.* HERBERT A. COCHRANE AND LUDWIG GROSS, Staten Island, N. Y. Arch. Int. Med. *89*: 82-89, January 1952.

In the case reported, the patient, a woman 52 years of age, showed signs and symptoms of hypersplenism, which were completely relieved by splenectomy. She remained well for more than a year and then was found to have chronic lymphatic leukemia. Serologic tests for syphilis were positive, but there was no clinical evidence of the disease, nor any evidence that the hypersplenism was of syphilitic origin. It is suggested that an increased hormonal activity of the spleen was induced by some unknown stimulus; by removal of the spleen, this organ's large collection of reticuloendothelial cells was also removed, but splenectomy did not eliminate the unknown primary stimulus, which continued to act on the remaining reticuloendothelial system, possibly genetically predisposed, affecting the balance of "acting substances" and eventually resulting in lymphoid metaplasia.

This is a "speculative conception" of this case, but it can be correlated with Wiseman's theory in regard to the role of the reticuloendothelial system in the production of leukemia. 19 references. 4 figures.

117. *Viremia in Acute Hemolytic Anemia and in Autohemagglutination.* SYLVAN E. MOOLTEN AND ELLEN CLARK, New Brunswick, N. J. Arch. Int. Med. *89*: 270-92, February 1952.

In a case of acute hemolytic anemia in a woman 37 years of age, a marked degree of autohemagglutination was found in attempting to type and cross match the patient's blood for transfusion. During the acute stage of the disease, an eruption resembling lupus erythematosus developed. After the acute phase subsided, the virus of Newcastle disease was isolated from the patient's blood and an increasing titer of heat-stable neutralizing antibodies and hemagglutination-inhibiting antibodies was demonstrated in the serum. A review of the literature indicates that hemotoxic viruses may be the cause of acute hemolytic anemia more frequently than has been suspected and that in cases with hemolytic or hemagglutinative phenomena clinically manifested as hemolytic anemia or atypical vascular syndromes (such as Raynaud's syndrome), and demonstrable in the laboratory, the examination of the blood for the presence of a hemotoxic virus would be justified. In the authors' preliminary study of 17 other cases in which autohemagglutination was demonstrated *in vitro*, a hemagglutinating virus was found in 14 instances. 91 references. 3 tables.

These are stimulating studies which, when confirmed, will contribute a great deal to knowledge on acquired hemolytic anemia as well as a new technic for identification of certain virus infections.—E. B. S.

118. *Hemolytic Anemia in Viral Pneumonia with High Cold-Agglutinin Titer.* ROBERT S. AARON, Brooklyn, N. Y. Arch. Int. Med. *89*:293-96, February 1952.

In a patient with viral pneumonia, a hemolytic anemia developed during the course of the disease. In this patient the cold-agglutinin titer was very high in the acute phase of the disease, and slowly returned to normal. The author suggests that in cases of hemolytic anemia of unknown origin, determination of the cold-agglutinin titer should be made. 12 references. 1 table.

119. *Oral Administration of Vitamin B_{12} Concentrate in Tropical Sprue and Nutritional Macrocytic Anemia.* R. RODRIGUEA-MOLINA, E. A. RAMIREZ-RODRIGUEZ, CARLOS E. ACEVADO, U. LOPEZ, JOSE M. TORRES, AND J. A. OLIVELLA, San Juan, Puerto Rico. Acta Haemetalogica *6*:277-83, November 1951.

Vitamin B_{12} concentrate, in amounts varying from 25 to 300 μg. daily, orally administered over periods of 5 to 7 days to two cases of acute sprue and to one case of nutritional macrocytic anemia, produced no significant hematopoietic response, and questionable clinical improvement. One case of chronic sprue presented slight subjective improvement but questionable hematologic response. When 150 and 300 μg. daily were administered to a case of pernicious anemia in relapse, a rapid sustained hematologic and clinical improvement was observed. However, no im-

provement in the long standing neurologic status was noted. 1 reference. 4 figures.—*Author's abstract.*

120. *Agranulocytosis in a Patient Treated with Mercurial Diuretics.* JACOB J. SILVERMAN AND JOSEPH F. WORTHEN, Staten Island, N. Y. J. A. M. A. *148*: 200-03, Jan. 19, 1952.

Mercurial diuretics are of prime importance in the management of congestive circulatory failure. Nevertheless, undesirable and toxic effects, including fatalities, are occasionally recorded. A 59 year old patient was carefully studied and found to be sensitive to salyrgan®-theophylline and mercuhydrin®. This sensitivity was characterized by an unusual depression of the white blood cells but was not observed with thiomerin®. At the height of the disorder, the peripheral blood was characterized by severe neutropenia and the bone marrow by a maturation arrest of the granulocyte series at the myelocyte stage. The mercurial diuretics may be added to the list of drugs capable of producing agranulocytosis. 9 references. 2 tables.—*Author's abstract.*

121. *Pernicious Anemia Superseded by Polycythemia Vera: Report of a Case.* JABEZ GALT, RICHARD B. HUNTER AND JOSEPH M. HILL, Dallas, Texas. Am. J. M. Sc. *223*:61-64, January 1952.

The change from pernicious anemia to polycythemia vera was observed in a 73 year old white female while receiving customary therapy for pernicious anemia. Panmyelosis progressed after discontinuing antianemic therapy, and the hemoglobin rose to 20 gma and the red blood cells to almost 14 million. There was an excellent response to therapy with radioactive phosphorus.

Thorough studies proving the existence of the two diseases were made. 8 references. 1 figure.—*Author's abstract.*

allergy

122. *Medical Progress: Allergy to Drugs.* EDWARD A. CARR, JR. New England J. Med. *245*:892-900, 935-40, Dec. 6 and 13, 1951.

This is a review article, discussing the various drugs, including antibiotics, that cause allergic reactions. The symptoms in drug allergy include those seen in allergy to proteins and other manifestations that are not characteristic of protein allergy, such as bone marrow depression manifested by agranulocytosis. The treatment of severe allergic reactions to drugs includes the same measures as are employed in severe protein allergies, as well as the antihistamines. If severe reactions persist, ACTH or cortisone is indicated; as such allergic reactions "represent a temporary situation," in which the prolonged administration of ACTH or cortisone is not

necessary, this type of allergy may prove to be one of the most rational indications for the use of these hormones. 262 references. 2 tables.

metabolic and endocrine disorders

123. *Induction of Thyroid Cancer in the Rat by Radioactive Iodine.* R. C. GOLDBERG AND I. L. CHAIKOFF, Berkeley, Calif. Arch. Path. *53*:22-28, January 1952.

In seven of 25 rats that had received single intraperitoneal injections of 400 microcuries of I^{131}, carcinoma of the thyroid gland developed 1.5 to 2 years later. Metastases, especially to the lung, were found in five of the seven rats with thyroid carcinoma.

One hundred twenty-five rats were examined after 18 to 32 months of being fed a goitrogenic diet containing propyl-thiouracil, to determine if prolonged pituitary thyrotropic hormone secretion might be the cause of the thyroid gland cancer. Although atypical discrete thyroid adenomata were noted, no metastasizing cancers were found.

The authors conclude that the ionizing radiation of I^{131} and not the effect of prolonged thyrotropic hormone is the cause of the thyroid cancer. 7 references. 3 figures. 2 tables.

124. *Origin of Urinary Creatine in Progressive Muscular Dystrophy.* MARCEL ROCHE, JEAN D. BENEDICT, T. F. YU, EDWARD BIEN AND DE WITT STETTEN. Metabolism *1*:13-19, 1952.

Heavy creatinuria is a cardinal manifestation of progressive muscular dystrophy. The isotopic composition of urinary creatine and creatinine was investigated in 2 normal male subjects and in 1 subject with severe progressive muscular dystrophy after the ingestion of isotopic (N^{15}) glycine. The urinary excretion of isotopic creatine was much greater during the first few days than the excretion of isotopic creatinine. Since the urinary creatinine excretion is a measure of muscle creatine content, the excessive isotopic creatine as compared to isotopic creatinine excretion indicates that most of the urinary creatine represents normally synthesized creatine that failed to enter the striated muscle. This failure is attributed to the discrepancy between an approximately normal rate of creatine formation and a diminution in functional muscle mass. Creatinuria, thus, is the result of the disease rather than an expression of a basic defect. 15 references. 3 figures.

125. *Determination of Serum Protein-Bound Iodine as a Routine Clinical Procedure.* BERNARD L. HALLMAN, PHILIP K. BONDY AND MARY ANN HAGEWOOD, Atlanta, Ga. Arch. Int. Med. *87*:817-24, June 1951.

Experiments at the Emory University Hospital with serum protein-bound iodine are presented. The mean normal value among normal subjects was 5.4 micrograms per 100 ml., with a standard deviation of 1.08 micrograms. Among hyperthyroid

patients, protein-bound iodine was increased, and it was below normal range in hypothyroid individuals. Pregnancy was associated with elevation of protein-bound iodine levels, with a mean of 10.2 micrograms and a standard deviation of 1.2 micrograms. Errors which might occur due to previous ingestion or administration of iodine-containing dyes or compounds or to the inadvertent introduction of iodine (tincture of iodine on the skin or exposure of the serum to iodine when permitted to stand in the laboratory) are discussed.

The protein-bound iodine was found to have certain advantages over the metabolic rate in that it can be obtained at any time of the day, does not require the patient to be in a "basal" state, and is uninfluenced by nervousness or fever. Where a basal metabolic rate could not be performed, as in thyrotoxicosis, congestive heart failure, or in mentally disturbed or pediatric patients, the protein-bound iodine determinations were found to be of definite value. The disadvantages were that previous administration of various diagnostic measures, such as intravenous pyelography, gallbladder dyes, or radiopaque oils for bronchography, may influence these tests. Gallbladder dye was found to cause abnormally high values for as long as 6 months whereas renal excretory dyes were eliminated rapidly and their effect would disappear within 3 to 4 weeks. After administration of inorganic iodides the protein-bound iodine would remain elevated for as long as 30 days and in instances for a longer period. The combination of the basal metabolic rate and protein-bound iodine determination was considered more useful as a routine measure than radioactive iodine uptake. 8 references. 3 figures.

126. *Incorporation of Glycine Nitrogen into Uric Acid in Normal and Gouty Man.* JEAN D. BENEDICT, MARCEL ROCHE, T. F. YO, EDWARD J. BIEN, ALEXANDER B. GUTMAN, AND DE WITT STETTEN. Metabolism, Clinical and Experimental *1*: 3-12, 1952.

The increase of the miscible pool of uric acid in gout may be due either to impaired elimination, decreased destruction or excessive generation of uric acid. Since glycine serves as a precursor to uric acid, the rate of synthesis of uric acid was measured in 1 gouty and 2 normal subjects after ingestion of isotopic (N^{15}) glycine. The urinary excretion of isotopic (N^{15}) glycine, urea, ammonia, and uric acid was measured daily.

The excretory pattern for isotopic nitrogen in the urinary total N, urea N and ammonia N were similar in the three subjects. However, the pattern for uric acid in the gouty subject differed markedly from the normal. The N^{15} concentration in urinary uric acid attained a higher maximum and declined more rapidly than normal and the fraction of isotope that was excreted as uric acid was far greater in the gouty than in the normal subject.

The authors conclude that there is in the gouty subject a more rapid mechanism for the transformation of dietary glycine into uric acid than in the normal subject. Also that the overproduction of uric acid is largely responsible for the pathologic increase in the size of the miscible pool of uric acid in this disease. 26 references. 5 figures.

127. *Influence of Potassium on Tissue Protein Synthesis.* PAUL R. CANNON, LAURENCE E. FRAZIER, AND RANDOLPH H. HUGHES, Chicago, Ill. Metabolism *1*: 49-56, January 1952.

Experiments designed to determine the influence of dietary potassium on the processes of tissue protein repletion indicated the necessity of this cation in the reconstruction of tissue protein. In protein-depleted rats, a ration adequate in calories, vitamins, amino acids, and salts effected a recovery of the lost weight. Removal of the potassium from the salt of this ration led to poor food consumption, failure to gain weight adequately, development of cardiac lesions characteristic of potassium deficiency, and early death. However, the addition of small amounts of potassium chloride to the deficient ration enabled the animals to achieve protein repletion quickly.

The authors point out that two protein hydrolysates of excellent amino acid composition failed to accomplish effective protein repletion in the absence of potassium salts. This indicates a critically low level of potassium in these hydrolysates and a consequent need for potassium supplementation.

128. *Adrenalin Sensitization Induced by Experimental Hyperthyroidism.* PENITTI PELTOLA, Helsinki, Finland. Acta med. Scandinav. Supp. 262:34-35, 1951.

The author reports that the minimal lethal dose of subcutaneous adrenalin was determined in control and hyperthyroid mice. The hyperthyroidism was induced by the ingestion of thyroid powder. The M.L.D. for normal mice is 7 gamma of adrenalin per Gm. of mouse; the M.L.D. is only 1 gamma per Gm. for the hyperthyroid mouse. The onset of sensitization is slow, and the maximum was not reached until 12 days of thyroid feeding.

The author suggests that the sudden deaths associated with surgical procedures in hyperthyroid patients may be attributed to adrenalin sensitivity.

129. *Hypercholesterolemia with Predisposition to Atherosclerosis; an Inborn Error of Lipid Metabolism.* DAVID ADLERSBERG, New York, N. Y. Am. J. Med. *11*:600-14, November 1951.

In a study of 500 consecutive admissions to a large general hospital, and their families, hereditary hypercholesterolemia was discovered in 4 to 5 per cent; a high incidence of this abnormality was found in Jewish families. From a study of these cases and a review of the literature, the author concludes that in most cases in which coronary atherosclerosis occurs early in life, there is a disturbance of lipid or lipoprotein metabolism that is hereditary. In the most severe form of this hereditary metabolic fault, xanthochromatosis is associated with the coronary atherosclerosis; early coronary atherosclerosis without xanthomatosis represents a milder form of the same hereditary metabolic fault. The patients in the first group carry two genes for this hereditary fault (homozygotes), while those in the second group carry only one gene for this metabolic fault (heterozygotes). 74 references. 1 table. 8 figures.

130. *Effect of Cortisone and ACTH on Fluid and Electrolyte Distribution in Man.* MARTIN F. LEVITT AND MORTIMER H. BADER, New York, N. Y. Am. J. Med. *11*:715-23, December 1951.

A study of fluid and electrolyte distribution, including measurements of inulin space, were made in 7 patients given cortisone (100 to 150 mg. daily) or ACTH (100 mg. daily) for 10 to 20 days. There was a shift of water, sodium, and chloride into the inulin space (extracellular volume), which reached the peak in eight to nine days of hormone therapy and then regressed, although treatment was continued. It also was found that both cortisone and ACTH caused an increase in glomerular filtration rate and filtration fraction, the maximum effect coinciding in time with the maximum changes in fluid distribution in the body. In 1 case in which mercuhydrin was given before the expected peak of the fluid shift, the resulting diuresis did not alter the changes in fluid distribution significantly. There was a moderate sodium and chloride diuresis but little diminution of the extracellular electrolyte. 47 references. 3 figures. 1 table.

131. *Essential Lipemia, Acute Gout, Peripheral Neuritis, and Myocardial Disease in a Negro Man.* JOHN K. FULTON, Wichita, Kan. Arch. Int. Med. *89*:303-08, February 1952.

In the case reported (a Negro male, 49 years of age), there were three metabolic diseases: essential lipemia with xanthomas, acute gout, and peripheral neuritis. There also was some myocardial abnormality, as shown by the electrocardiogram, but no symptoms of cardiac disease. Treatment with corticotropin (ACTH) in a dosage of 20 mg. every six hours until a total of 560 mg. had been given relieved the symptoms of gout and of peripheral neuritis. The patient was given a low-fat diet and colachine 1/100 grain three times a day. A month later he had returned to work and the xanthomas were disappearing; two months later he was entirely free from symptoms and the xanthomas had completely disappeared. There was apparently a relationship between the lipemia and the gout, since increase in blood lipids is known to have an unfavorable influence on gout and both hyperlipemia and gout are favorably influenced by corticotropin. The relationship between the lipemia and peripheral neuritis is not so evident, but as diabetic neuritis is sometimes correlated with disturbances of blood lipids, there may have been a similar relation in this case, especially since the neuritis was also relieved by corticotropin therapy. 14 references. 2 figures.

132. *A Critical Analysis of the Quantitative I^{131} Therapy of Thyrotoxicosis.* A. STONE FREEDBERG, GEORGE S. KURLAND, DAVID L. CHAMOVITZ AND ALVIN L. UREles, Boston, Mass. J. Clin. Endocrinol. *12*:86-111, January 1952.

This investigation was undertaken to ascertain: (1) whether the thyroid uptake and turnover (biologic half-life) following a therapeutic dose of I^{131} was predictable from the uptake and turnover following a tracer dose and (2) the relationship between the estimated radiation delivered by the therapeutic dose of I^{131} and the

therapeutic effect. The method utilized for measurement of thyroid uptake and turnover by external counting consisted of four Geiger-Mueller tubes connected in a parallel electrical circuit and arranged in a circle of 45 cm. radius in a horizontal plane about the neck. This method provides quantitative measurement of I^{131} thyroid gland content, virtually independent of the size and location of the thyroid gland.

In 53 comparisons of tracer and therapeutic doses in 42 patients with thyrotoxicosis, the average uptake of the tracer dose, 24 hours after I^{131} administration, was 72.7 per cent (S.E., 1.8 per cent), and the average uptake of the therapeutic dose was 72.4 per cent (S.E., 2.4 per cent). The average difference between the 24 hour uptake measured after a therapeutic dose and that measured after the tracer dose in the same patient was 8.6 per cent (S.E., 1.7 per cent).

In five of the 53 comparisons, the uptake of the therapeutic dose differed from that of the tracer dose by 20 per cent or more. In four of these five instances, the probable source of the discrepancy was either the recent omission or the administration of stable iodide (potassium iodide and organic iodo compounds or of antithyroid drugs between the tracer and therapeutic doses).

The average biologic half-life following the tracer dose was 5.5 days (S.E., 1.7) and following the therapeutic dose, 5.5 days (S.E., 1.5). The average difference between the biologic half-life measured after the therapeutic dose and that found after the tracer dose in the same patient was 11.5 per cent (S.E., 1.4 per cent).

In 11 instances in 10 patients, the difference between the biologic half-life of a therapeutic dose and that of its corresponding tracer dose was 20 per cent or greater. In 8 of the 11 the biologic half-life of the therapeutic dose was shorter than that of the corresponding tracer dose; in the remaining 3 it was longer. In 1 case, the difference was due to the administration of Diodrast between the tracer and the therapeutic dose; no adequate explanation is available for the differences observed in the other cases.

The predictability of the delivered thyroid radiation of a therapeutic dose, on the basis of the uptake and biologic half-life, following a tracer dose, is sufficiently accurate to allow for calculated I^{131} dosage. In 50 comparisons made in 40 patients, the REP delivered by the therapeutic dose to the thyroid gland differed from that anticipated on the basis of the tracer studies by an average of 16.8 per cent (S.E., 1.8 per cent).

Evaluation of the relationship between delivered radiation and therapeutic effect was possible in 36 of the 42 patients. Twenty-six of the 36 patients received only one therapeutic dose of I^{131}, ranging from 2.7 to 25.0 millicuries; 20 patients were euthyroid after an estimated thyroid radiation of 5,800 to 17,000 REP (average, 9,700). The remaining 6 patients, receiving one dose, became hypometabolic after a thyroid radiation of 8,000 to 19,100 REP (average, 10,900); 5 of the 6 received less than 10,000 REP. There was considerable overlap of dosage in these two groups.

Ten of the 36 patients, though improved, remained thyrotoxic after an initial thyroid radiation ranging from 5,000 to 12,500 REP (average, 8,800). Five of the 10 have been rendered euthyroid with a total radiation of 11,300 to 37,500 REP de-

livered in two to four doses totalling 5.6 to 38.0 millicuries. Two have become hypothyroid after a total dosage of 17,000 to 19,300 REP delivered by two doses totalling 12.3 and 5.3 millicuries. One patient has remained persistently mildly thyrotoxic after three doses of I^{131}, totalling 28.1 millicuries, estimated to have delivered 32,800 REP. Thus, of the 34 patients in whom comparison of total thyroid radiation and therapeutic effect was possible, 25 (73 per cent) are euthyroid, 8 (24 per cent) are hypothyroid, and 1 presents persistent mild thyrotoxicosis. The greatest incidence of hypothyroidism and a high incidence of persistent thyrotoxicosis or myxedema after administration of I^{131} was at least in patients whose thyroid glands were estimated to weigh less than 50 grams.

The thyroid uptake and turnover (biologic half-life) of a therapeutic dose of I^{131} can be determined from the uptake and turnover following a tracer dose.

The predictability of the delivered thyroid radiation of a therapeutic dose of I^{131}, on the basis of the uptake and biologic half-life following a tracer dose, is sufficiently accurate to allow for calculated I^{131} dosage. 27 references. 5 figures. 3 tables.—*Author's abstract.*

dermatology and syphilology

133. *Use of Neomycin in Dermatology.* ROY L. KILE, EVELYN M. ROCKWELL AND JAN SCHWARZ, Cincinnati, Ohio. J. A. M. A. *148*:339-43, Feb. 2, 1952.

Topical application of this antibiotic on over 700 patients has been found most effective in a number of skin infections. Several ointment bases were evaluated, including an ophthalmic ointment; likewise, wet compresses of a solution of the drug, and in a few cases, injections of neomycin.

A greasy-type ointment was found most effective and gave the fewest reactions attributable to the base itself.

Patch tests with each type of ointment were done on 140 persons. A single reaction was proved due to the water miscible base and not to the neomycin. Retesting of the same group was repeated two weeks later.

Bacteriologic studies were carried out on 150 patients. Organisms were tested for sensitivity to the antibiotic. Only one proven case of sensitivity to this antibiotic was observed in this series. Due to its low sensitizing index and effectiveness against a wide spectrum of organisms, we are impressed that neomycin is about the best antibiotic for topical application against skin infections. 12 references. 1 table.—*Author's abstract.*

134. *Terramycin. A New Antisyphilitic Medication.* C. LEVADITI AND A. VAISMAN, Paris, France. Antibiotics and Chemotherapy *1*:425-30, October 1951.

Terramycin appears to be an antisyphilitic medication of the first order. Its therapeutic effects are manifested in the rabbit by rapid immobilization of *Treponema pallidum* in the scrotal syphilomas and their early disappearance, as well as by prompt healing of these syphilomas and, finally, by sterilization of the blood

and of the popliteal glands 12 and 15 days following the initiation of treatment. The same therapeutic effects apply to mice and can be verified by microscopic sterilization of dispersed treponemosis from the eleventh or twelfth day on.

From this viewpoint, terramycin therefore approximates penicillin. Nevertheless, only by carrying out comparative tests with precise dosages will it be possible to evaluate properly the antitreponemic activity of these two antibiotics. Our forthcoming studies will deal with this problem as well as with the problem of the terramycin-bismuth combination.

135. *Current Concepts of Beryllium Poisoning.* H. S. VAN ORDSTRAND, Lancaster, Pa. Ann. Int. Med. *35*:1203-17, December 1951.

Beryllium poisoning is one of the newer occupational diseases. There is much to suggest that it causes systemic involvement, rather than merely a pulmonary lesion, its most severe manifestation. It is a condition which should stimulate the internist to further cooperation with industrial medicine.

Beryllium has been called the "glamour child" of metallurgy. The multiple usage of it and its compounds and alloys has been discussed. The author and his colleagues have had the opportunity of observing all of the clinical manifestations of beryllium poisoning since 1940. Examples of each are shown, including the clinical and pathologic findings.

A summary of the extensive and excellent research work being carried out in various parts of the country and elsewhere is presented. It has been demonstrated clearly that the eczematous contact type dermatitis in beryllium workers is a hypersensitization phenomenon. There is much to suggest that the acute beryllium lung problem may also be an allergic reaction. Facts and theories have been presented as to the pathogenesis of the chronic granulomatous form of the disease. Independent research conducted at three places in this country and one in Great Britain suggests that beryllium has an inhibitory effect on the alkaline phosphatase enzymes. The hypothesis that beryllium may compete for magnesium in magnesium-activated enzymes may provide an explanation of the toxic properties of beryllium, although much remains to be clarified. Expansion of our knowledge of this occupational disease may give basic clues to the body's reactions in the large group of granulomatous diseases.

Multiple treatments have been employed, but no specific antidote has been found. ACTH and cortisone therapy have been encouraging and have produced noticeable symptomatic benefits; they have proved to exert a regressive influence in a number of patients demonstrating the chronic and progressive granulomatous forms of the disease.

A remarkable reduction in the incidence of beryllium poisoning has occurred since the institution of safety engineering and industrial hygiene in the involved industries.

136. *Occupational Dermatoses in Physicians.* ERVIN EPSTEIN, Oakland, Calif. J. A. M. A. *147*:1751-54, Dec. 29, 1951.

The findings presented in this article are based on answers by 60 leading dermatologists to a questionnaire. Contact dermatitis seemed to be the most common type of reaction suffered and the common specific causes included scrubbing, rubber gloves, local anesthetics, antiseptics and antibiotics. Five contributors felt that the psychosomatic aspect was important in such cases. Among the infections, pyodermas were most frequently noted, although virus, parasitic and venereal diseases were also reported. Twenty seven instances of extragenital chancres in physicians were gathered during this survey; three cases of inoculation tuberculosis were found. However 40 per cent of the dermatologists reporting stated that they had seen no infections of any kind in physicians resulting from contact with patients. Radiodermatitis is still occurring, but is due to negligence and is considered to be inexcusable. It is also pointed out that as a group, physicians are uncooperative and impatient in dealing with their own dermatoses. The dangers of overtreatment are stressed. The acceptance of suggestions as to antihistaminics, antibiotics and adrenal steroids for self-treatment is deplored.—*Author's abstract.*

137. *Skin Lesions in Association with Ulcerative Colitis.* M. H. SAMITZ AND M. S. GREENBERG, Philadelphia, Pa. Gastroenterology *19*:476-79, November 1951.

The Department of Dermatology of the Graduate Hospital reviewed the records of cases of ulcerative colitis admitted to the gastroenterology service over a twenty year period (1930–1950). To compile statistics for this report, the records of 189 patients representing 318 hospital admissions were surveyed. This sample represented 67 per cent of both the individual patients and of the total admissions for ulcerative colitis during that time.

In the previous literature, there is reported an incidence of skin lesions complicating ulcerative colitis of from 2 to 9 per cent. In this survey 34 per cent of the 189 individual patients had one or more skin complications.

The causal mechanisms attributed to the production of these dermatologic entities, namely, allergic, toxic, bacterial, viral, and psychosomatic, are similar to those agents proposed in the etiology of ulcerative colitis. The histologic picture of these different skin conditions at times parallels the histology of various stages of ulcerative colitis. With such a relationship, one postulates what type of skin lesions are produced by the same mechanism, whether there is a sequence relationship, or whether the skin merely reflects the altered process in a primary focus in the colon. The inter-relationship of the etiology and pathology of these skin patterns and that of ulcerative colitis is suggestive, but the verification of particular factors remains unestablished. It is hoped, however, that further investigation of this problem should be stimulated and perhaps the skin may shed light on the behavior of ulcerative colitis. 4 references. 3 tables.—*Author's abstract.*

138. *Papilloma of the Umbilicus.* SIDNEY VERNON, Willimantic, Conn. J. A. M. A. *147*:755-56, October 1951.

Papilloma of the umbilicus is a benign asymptomatic lesion which becomes conspicuous when infection develops. The malignancy potential of the lesion and the possibility of congenital anomaly require diagnostic study. Biopsy should be done. Oral methylene blue is given to check for urinary bladder continuity through a patent urachus. Carmine red chalk is given by mouth to check for connection with the bowel through a patent vitelline duct.

Occurrence of the lesion may follow a delay of healing of the umbilicus in the neonatal period. It commands attention when pain, itching, and discharge follow infection. This may occur at any time of life when local hygiene is inadequate.

The papillary projections are covered by keratinized epithelium of normal thickness and have a connective tissue core. Rete pegs contain pearls of keratin and are elongated into intricate lacy folds. The predominant cell is the prickle cell of the *stratum mucosum.*

A case is reported in which surgical excision of the umbilicus *en masse* removed the threat of a premalignant lesion and the abnormality that made local cleanliness difficult. This is the fifteenth reported case.

139. *Cortisone and Corticotropin (ACTH) in Dermatology.* ROBERT R. KIERLAND, PAUL A. O'LEARY, LOUIS A. BRUNSTING AND JOHN W. DIDCOCT, Rochester, Minn. J. A. M. A. *148*:23-26, Jan. 5, 1952.

This report summarizes the experience of the Mayo Clinic group in the treatment of dermatologic conditions with corticotropin (ACTH) and/or cortisone. Potential physiologic side effects and changes in the psyche were discussed. However, few of our patients showed any of these alterations to a significant degree. Some of those who had disseminated lupus erythematosus had a marked degree of fluid retention and hypopotassemia. For the majority of patients with dermatoses the courses of treatment were short, and significant physiologic alterations were seldom seen. Two patients became frankly psychotic for a brief period but completely recovered in two to four weeks after withdrawal of treatment. Thrombophlebitis may develop in patients receiving cortisone. Emphasis is made of the ability of these hormones to suppress the symptoms and surface signs of infectious disease and this action may prevent the recognition of unexpected infections in patients. This masking effect has been encountered in peritonitis, pneumonococcic septicemia, miliary tuberculosis and encephalitis.

No benefit was seen with the local use of cortisone in cutaneous conditions. From an analysis of our results these hormones are recommended on the basis of the relief of symptoms but not on the basis of a cure. Worthwhile results have been obtained in cases of acute lupus erythematosus, early scleroderma, pemphigus vulgaris, pemphigus foliaceus, psoriatic arthritis, certain forms of exfoliative dermatitis, drug and serum reactions, and for the intense pruritus of some eczematous states. In patients with dermatomyositis our initial experience was discouraging. However, one later patient showed a marked degree of improvement. Syphilitic

interstitial keratitis is influenced remarkably by the local instillation of a 1 to 2 per cent suspension of cortisone. These hormones are not considered efficacious at this time for uncomplicated psoriasis, the usual eczematous patient or for lymphoblastoma of the skin. On occasions when ACTH or cortisone is considered for the treatment of eczematous conditions, it is suggested that the treatment be reserved for patients with intractable symptoms and that courses of treatment be of short duration. Such patients have a tendency to become dependent upon the hormone for relief. In all cases an effort should be made to find the minimal maintenance dose that provides suppression and relief of symptoms. These hormones should not be administered promiscuously, without knowledge of their physiologic effects and dosage and without knowledge of the influence of infection upon those receiving such treatment. 7 references.—*Author's abstract.*

diseases of doubtful origin

140. *Chronic Panniculitis with Leucopenia* (*Weber-Christian Syndrome*). HEYWORTH N. SANFORD, DAVID F. EUBANK AND FREDERICK STENN, Chicago, Ill. Am. J. Dis. Child. *83*:156-63, February 1952.

A fatal case of chronic nonsuppurative panniculitis with leukopenia is reported in an eight and one-half month old infant. This condition is characterized by recurrent crops of subcutaneous nodules which occur during febrile periods, and shows by histologic examination a particular kind of fat atrophy. Weber described this condition in 1925.

The child was perfectly well until six months of age, when the skin lesions developed, with fever of 100 to 102 degrees. While the general nutrition remained good, the child became more toxic and died despite treatment with penicillin, aureomycin, ACTH, and transfusions.

This is the youngest case reported in the pediatric age group under eleven years of age in American and English literature and is the fifty-seventh case reported in all ages.

It is the second recorded instance in which a bacterial organism (*Streptococcus viridans*) has been cultured from the subcutaneous nodules as a possible etiologic agent.

The case was also found to have a cryoglobulinemia (albumin 61 per cent, globulins—alpha-1, 9 per cent; alpha-2, 10 per cent; beta, 11 per cent; and gamma, 9 per cent). While this finding has only been described in this one case, it may be of diagnostic importance.

From a review of the published descriptions of these cases, it is believed that Weber-Christian disease should be considered as a syndrome, and not a specific disease entity. It apparently occurs in conditions in which the subcutaneous fat is involved, without suppuration. The etiologic agent may be one of many factors. 25 references. 2 figures.—*Author's abstract.*

141. *The "L. E. Cell" and Its Significance.* PETER A. J. SMITH, Boston, Mass. Brit. J. Dermat. *64*:10-25, January 1952.

The nature of the so-called "L. E. Cell," the methods that have been used for its demonstration, and the properties of the serum-factor upon which its production depends, are reviewed. The demonstration of the L. E. phenomenon is not only a specific diagnostic test for systemic lupus erythematosus, but should also help to throw light on the underlying pathogenesis of the disease.

Six cases are described to illustrate the different clinical pictures that may be called systemic lupus erythematosus, and to show that not every undoubted case of that disease gives rise to the L. E. phenomenon. 57 references. 5 figures. 1 table.—*Author's abstract.*

basic sciences

142. *Distribution and Excretion of Electrolytes After Acute Whole-body Irradiation Injury. I. Studies with Radiopotassium.* JOHN Z. BOWERS AND KENNETH G. SCOTT, San Francisco, Calif. Proc. Soc. Exper. Biol. & Med. *78*:645-48, November 1951.

Rats show a substantial loss of potassium from a majority of radiosensitive tissues beginning within 24 to 48 hours after irradiation. There is a comparable loss from the bones. Radio-potassium excretion is increased in the urine of irradiated rats, and there is a rise in the fecal levels with the onset of diarrhea. It is evident that rats that have been irradiated at over an LD_{50} level develop an absolute potassium deficiency. The loss of potassium from radio-resistant bone may indicate a movement of potassium out of the bone lattice or a loss of potassium from osteoblast cells, which are considered the most sensitive of the bone cells. If this is correct, the findings would suggest that osteoblasts are as sensitive to irradiation injury as the cells of the hematopoietic system.

Dehydration, diarrhea, total anorexia, and shock after whole-body irradiation injury in humans are associated with depletion of intracellular potassium, especially in muscle. Considering the severity of these manifestations in irradiation injury, it seemed puzzling not to be able to detect more significant changes in the potassium concentration of muscle during the 72 hours of the experiment. It is suggested that potassium from the tissues appears rather promptly in the urine and that the kidney does not conserve potassium in situations of developing intracellular deficit. Thus, total anorexia, depletion of potassium in a number of tissues, and increased loss in the urine and stools contribute to absolute potassium deficiency in these animals. 6 references, 2 figures, 2 tables.

143. *Distribution and Excretion of Electrolytes After Acute Whole-body Irradiation Injury. II. Studies with Radiosodium.* JOHN C. BOWERS AND KENNETH G. SCOTT, San Francisco, Calif. Proc. Soc. Exper. Biol. & Med. *78*:648-52, November 1951.

The changes in sodium metabolism following acute whole-body irradiation injury are described. The relation of changes in radio-sodium concentration to irra-

diation injury is more difficult to estimate, since they do not coincide with changes in percentage water content. Some of the striking increase in sodium concentration in radiosensitive tissues is partly due to penetration into cells that have been injured by irradiation and from which there has been an extensive loss of potassium. There is no correlation between changes in the percentage of water content and in dry weight in organs after irradiation. The marked increase in the dry weight of the spleen is puzzling and may represent a pooling of formed elements of the blood in this organ and an accumulation of debris.

Radiosensitive tissues show a variety of alterations in radio-sodium concentration after total body irradiation above an LD_{50}. In several tissues, a preliminary decrease is followed by a sharp increase. The decrease occurs at the same time as the decrease in radio-potassium concentration. The percent loss of dry weight per day is in general most pronounced in radiosensitive tissues. The urinary excretion of radio-sodium after total body irradiations at levels approximating an LD_{50} shows a complementary homeostatic decrease in response to the excessive loss of radio-sodium through the gastrointestinal tract. This report concerns the pattern of urinary and fecal excretion of sodium in rats after acute, whole-body irradiation with X-rays and the accompanying changes in sodium concentration in tissues and organs. 9 references. 1 figure. 3 tables.

144. *N, N'-Dibenzylethylenediamine Penicillin: Preparation and Properties.* J. LESTER SZABO, CHARLES D. EDWARDS AND WILLIAM F. BRUCE, West Chester, Pa. Antibiotics and Chemotherapy *1*:499-503, November 1951.

The preparation of N, N'-dibenzylethylenediamine and some of its salts is described. Ethylenediamine was condensed with benzaldehyde, 60 Gm. of 90–95 per cent ethylenediamine was slowly added to 212 Gm. of benzaldehyde. After cooling, the water formed was poured off. The yield of N, N'-dibenzylethylenediamine was 188 Gm., m.p. 51.5–53°. The product 2060 Gm. was hydrogenated in two batches using 1 L. of methanol with 5 Gm. of platinum oxide. The crude product was treated with excess 10 per cent sulfuric acid and live steam to hydrolyze the 1, 3-dibenzyl-2-phenyltetrahydroimidazole (m.p. 97–98°) formed as a by-product, and to remove benzaldehyde formed as a hydrolytic product. The yield was 1313 Gm., b.p. 195–197° at 4-5 mm., N_D^{25} 1.5621. The diacetate was prepared from 440 Gm. of the base and 220 Gm. acetic acid and in 3 L. alcohol followed by recrystallization from alcohol, m.p. 110–112°, solubility in water 25.3 per cent. The lactate m.p. 74° prepared in alcohol was easily soluble in water. The melting points and percentage solubilities in water of salts follow: dihydrobromide 300°, 3.0; dihydrochloride, 298°, 2.39; dinitrate 274°, 0.9; diphosphate 232°, 3.86; sulfate 247–250°, 1.58; dithiocyanate 212°, 3.68; dioxalate 275–276°, disalicylate 85°, 0.24. The penicillin-G salt $C_{16}H_{20}N_2 2C_{16}H_{18}O_4N_2S$, white needles, m.p. 123–124°, $[\alpha]_D^{25}$ + 206° (0.105 per cent in formamide), assay about 1200 u./mg., whose solubility in water is about 0.016 per cent at room temperature, is much more soluble in formamide, dimethylformamide, soluble in ethanol and methanol, but only slightly soluble in acetone; this was prepared by treating an aqueous solution of 60 Gm. sodium penicillin with

a solution of 35 Gm. dibenzylethylenediamine diacetate. The finely divided product retained about 9 per cent moisture. By very slow addition of the reactants or better by precipitation from warm formamide, dimethylformamide or acetone aqueous solutions, larger crystals were obtained. 7 references. 4 tables.—*Author's abstract.*

145. *Determination of Stilbamidine and 2-Hydroxystilbamidine in Parenchymatous Organs and Tumors.* I. SNAPPER, F. LIEBEN, E. GREENSPAN AND B. SCHNEID, New York, N. Y. Cancer *4*:1246-49, November 1951.

It has been established that considerable amounts of stilbamidine and 2-hydroxystilbamidine are deposited in the parenchymatous organs, in particular in the liver, kidneys and adrenals. Frequently one-third of the quantity injected can be recovered from these organs. The deposition differs in different species. Thus, in mice the kidneys are found to contain more diamidine than the liver, while in man and rabbits the opposite is true. Mice bearing a transplantable hepatoma subcutaneously show larger amounts of diamidine in the liver and kidneys than normal mice. Following injection of these diamidines, considerable quantities are deposited in the transplantable hematoma. Indicating a certain specificity, it was observed that, following the same injections, the transplantable lymphosarcoma of the mouse showed only traces of the substance. This was true also of a transplantable mammary carcinoma. Once deposited in the liver and adrenals, the diamidines remain there for a long time. Appreciable amounts were recovered from the liver of a myeloma patient 23 months after the last injection of 2-hydroxystilbamidine. In another case marked traces could still be demonstrated in the liver 3 years and 3 months after the last injection. In mice the injections were made subcutaneously, in human subjects intravenously with a daily dose of 150 mg. and a total dose in most cases of 2–2.5 Gm. In some cases of myeloma much larger doses were administered.

The tumors in the 10 patients included 4 cases of multiple myeloma, one case of cirrhosis of the liver with hepatoma, one case of cancer of the thyroid with Hodgkin's disease, one case of polycythemia with thrombosis of the hepatic veins, one case of hepatoma, one case of myeloma with Paget's disease and one case of hypernephroma. 5 references. 1 figure. 12 tables.

146. *Production of Soluble Pigments by Certain Strains of Streptomyces Griseus.* ROBERT G. BENEDICT AND LLOYD A. LINDENFELSER, Peoria, Ill. Antibiotics and Chemotherapy *1*:512-17, November 1951.

Twenty-three strains of *Streptomyces griseus* were grown in simple synthetic media containing ammonium chloride and salts of various alpha-hydroxy and dibasic acids.

A majority of the streptomycin-producing strains formed a green soluble pigment only in calcium malate medium and a yellow pigment in calcium succinate. A grisein-producing strain formed a light pink pigment in calcium succinate and calcium malate, but produced no antibiotic, whereas two grisein-like producers

formed no pigments, but yielded appreciable amounts of antibiotic in these media.

These findings tend to separate further those *S. griseus* strains which form grisein and unclassified antibiotics from those strains which produce streptomycin. 11 references. 3 tables.—*Author's abstract.*

147. *Effect of Oral Terramycin Prior to Whole-body X-radiation.* GORDON E. GUSTAFSON AND SIMON KOLETSKY, Western Reserve University. Proc. Soc. Biol. & Med. *78*:489-90, November 1951.

Mortality in rats may be reduced following whole-body irradiation, if terramycin is administered for a period of only 48 hours prior to 660 r of whole-body irradiation. By changing the flora of the intestines, this treatment apparently reduces the incidence of bacteremia following radiation. Possibly an even greater effect may be noted if the drug is administered 72 rather than 48 hours before radiation. The 30-day mortality after 660 r when the drug was administered 72 hours before radiation was 32 per cent as compared with 86 per cent in control animals. Severe radiation injury is frequently associated with bacteremia, the intestinal tract appearing to constitute the main port of entry. The present study was undertaken to ascertain whether a reduction or alteration of intestinal flora by preliminary treatment with antibiotics might reduce the mortality rate. 8 references. 1 figure.

148. *Antigenic Similarity of Some Trained Resistant Strains of Viridans Streptococci to Streptococcus Fecalis.* MAXINE FELTZ AND WILLIAM E. CLAPPER, Denver, Col. Proc. Soc. Exper. Biol. & Med. *78*:491-92, November 1951.

Some strains of *Streptococci viridans* trained to resistance to sulfathiazole, penicillin and aureomycin, acquired many biochemical properties natural to enterococci. Such strains differed in their acquisition of such properties. An attempt was made to determine whether these resistant strains were antigenically related to the *Streptococcus fecalis.* This was found to be the case. The details of the experimental procedure are described. Sulfadiazine-sensitive *Streptococci viridans* do not have this property. Certain strains of *Streptococci viridans* may thus be induced to change to enterococci. 10 references. 1 table.

149. *Cross-Resistance to Antibiotics, Effects of Repeated Exposure of Bacteria to Aureomycin, Terramycin, Chloramphenicol, or Neomycin on the Resistance to all of these Antibiotics and to Streptomycin and Penicillin.* THOMAS M. GOCKE AND MAXWELL FINLAND, with technical assistance of CLARE WILCOX, Boston, Mass. J. Lab. & Clin. Med. *38*:719-35, November 1951.

Repeated exposures to aureomycin or terramycin resulted in the development of mutual cross-resistance to these agents most regularly and clearly. The results with chloramphenicol varied with the organism. Following exposures to that agent, some strains developed significantly increased resistance to aureomycin and/or terramycin, while others did not. Conversely, some strains rendered resistant to either aureomycin or terramycin also developed significantly increased resistance to chloramphenicol, while such was not the case with other strains.

Organisms rendered resistant to neomycin as a result of repeated subcultures on this antibiotic showed no increase in resistance to aureomycin, terramycin, or chloramphenicol, and in some instances appeared to become more sensitive to these three agents. Conversely, strains which had increased in resistance to aureomycin, terramycin, or chloramphenicol generally showed unchanged sensitivity to neomycin. Almost all of the strains which had increased in resistance to neomycin, however, also increased significantly and sometimes markedly in resistance to streptomycin.

None of the strains tested had changed in their sensitivity to penicillin as a result of repeated exposures to either aureomycin, terramycin, chloramphenicol, or neomycin.

A chloramphenicol-dependent variant of *Klebsiella pneumoniae*, which emerged in the course of this study, grew only in the presence of a narrow critical range of concentrations of that agent, and not in the presence of any of a wide range of concentrations of four other antibiotics. 10 references. 4 figures.—*Author's abstract.*

150. *Comparison of Methods for Determining Sensitivity of Bacteria to Antibiotics in Vitro.* GEORGE GEE JACKSON AND MAXWELL FINLAND, Boston, Mass. Arch. Int. Med. *88*:446-60, October 1951.

The sensitivity of seven organisms to six antibiotics was tested by several methods including various modifications of the methods that are most widely used.

Wide ranges of values were obtained for the minimum inhibiting concentrations of any one antibiotic for any given organism, depending on the method used. In particular, these values were shown to be influenced profoundly by the size of the inoculum, the period of incubation, and the choice of complete or partial inhibition as the endpoint of the tests. These factors affected the results differently depending on the combination of organism and antibiotic that was being tested.

The value and limitations of the results of tests for sensitivity of bacteria to antibiotics were discussed, particularly with respect to their clinical application. 12 references. 4 tables.—*Author's abstract.*

151. *Pharmacological Properties of A New Antispasmodic, N, N-Dimethylthymyloxyacetamidine Hydrochloride.* BRADFORD N. CRAVER, WALTER BARRETT, ANNE CAMERON, ALFRED E. EARL AND FREDERICK F. YONKMAN, Fort Wayne, Ind. Am. J. Digest. Dis. *18*:241–45, August 1951.

The activities of a new antispasmodic, N, N-dimethylthymyloxyacetamidine hydrochloride and of its diethyl congener have been compared with the corresponding activities of Trasentine, Trasentine-6H, and atropine sulfate in respect to the following: a. antagonism of a histamine-induced spasm of the ileum of the guinea pig; b. antagonism of an acetylcholine-induced spasm of the ileum of the guinea pig; c. antagonism of a barium chloride-induced spasm of the small intestine of the rabbit; d. actions on the feline uterus *in vitro* and *in vivo*; e. actions on the nictitating membrane of the cat and on salivation induced by drugs and by stimulation of the chorda tympani nerve; f. paralysis of the peripheral cut vagus in the cat;

g. antagonism of Mecholyl-induced hypotension in the cat; h. intravenous LD_{50} in white rats; and i. chronic toxicologic studies in dogs and rats.

The effects of Su-198 upon the intestines of dogs with Thiry-Vella loops and upon the bronchioles of the perfused guinea pig's lung have been described.

Some of the problems have been discussed which must be solved before an objective evaluation of an antispasmodic becomes possible. 5 references. 2 figures. 2 tables.—*Author's abstract.*

152. *The Toxicity of N, N'-Dibenzylethylenediamine (DBED) and DBED Dipenicillin.* JOSEPH SEIFTER, JEROME M. GLASSMAN, ALBERT J. BEGANY AND ALBERT BLUMENTHAL, Philadelphia, Pa. Antibiotics and Chemotherapy, *1*:504–08, November 1951.

The acute toxicity, irritant properties and local anesthetic actions of N, N'-dibenzylethylenediamine dihydrochloride and N, N'-dibenzylethylenediamine dipenicillin were compared with those of procaine hydrochloride and procaine penicillin by standard pharmacologic technics in mice, rats, guinea pigs, rabbits, dogs and frogs.

The toxicity of DBED dipenicillin compares favorably with procaine penicillin partly because the slow hydrolysis of the former permits prolonged absorption with adequate excretion and detoxication; also, one molecule of DBED combines with two molecules of penicillin, so that half as much base is necessary to achieve the same blood level as with procaine penicillin.

Dogs tolerate the intragastric administration of DBED dipenicillin better than they do procaine penicillin and experience less nausea and vomiting.

Neither DBED dihydrochloride nor the dipenicillin are any more irritating to ocular mucosae, skin, and muscle than procaine hydrochloride or procaine penicillin.

The local anesthetic action of DBED dihydrochloride compares favorably with that of procaine hydrochloride. DBED dihydrochloride and dipenicillin also appear to be devoid of cholinergic properties. 2 tables.—*Author's abstract.*

153. *Rimocidin, a New Antibiotic.* J. W. DAVISSON, F. W. TANNER, JR., A. C. FINLAY, AND I. A. SOLOMONS, Brooklyn, N. Y. Antibiotics & Chemotherapy *1*:289–90, August 1951.

A second antibiotic has been recovered from *Streptomyces rimosus*, producer of terramycin, and crystallized from aqueous methanol.

Crystalline Rimocidin is an amphoteric compound, characterized by UV absorption at 279, 291, 304 and 318 $m\mu$. It is active at circa 5μg/ml. against a variety of pathogenic fungi. It is not antibacterial.—*Author's abstract.*

154. *Antibiotic Activity of Selected Enteric Organisms.* VIRGINIA L. BLACKFORD, LELAND W. PARR AND MARY LOUISE ROBBINS, Washington, D. C. Antibiotics and Chemotherapy *1*:392–98, September 1951.

Forty-seven strains of enteric bacteria, isolated from human subjects, were tested for their antagonistic properties against a variety of gram-negative and gram-

positive organisms. Of these 51.1 per cent possessed some antagonistic activity. All tests were carried out on solid media, using an agar pour-plate technique. During the course of experimentation certain other phenomena were noted and a partial study of these was made. It was observed that the size of the zone of inhibition increased on standing at room temperature and that antagonistic activity could be inhibited by varying the constituents of the medium on which the colicine producers were grown. The possible significance of these findings is discussed. 6 references. 1 figure. 3 tables.—*Author's abstract.*

155. *A Simple Method for Determination of Levels of Amethopterin in the Blood and Urine.* JOSEPH H. BURCHENAL, GEORGIA B. WARING, ROSE RUTH ELLISON AND H. CHRISTINE REILLY, New York, N. Y. Proc. Soc. Exper. Biol. & Med. *78*:603-06, November 1951.

The marked variations in the amounts of amethopterin or other folic acid antagonists which different patients can tolerate suggests that there may be considerable differences in their ability to absorb and metabolize these compounds. In order to facilitate studies of the absorption and excretion of amethopterin, a simpler assay method than Swenserd's turbidometric method has been devised, similar to those used to determine levels of penicillin and streptomycin. The technic of the new method is described in detail, a simple disc technic for determining the concentration of amethopterin in the blood and urine. The accuracy of this method compares favorably with similar assay methods for antibiotics.

156. *Action of Forty-Five Antibacterial Substances on Bacterial Viruses.* ELIZABETH A. HALL, FREDERICK KAVANAGH, IGOR N. ASHESHOV, New York, N. Y. Antibiotics and Chemotherapy *1*:369–78, September 1951.

Forty-five substances, known to have antibacterial or antifungal properties were studied for their action on sixty different races of bacteriophage. The method used was the paper disc plate method which has been described in a previous report (Asheshov, I. N., Strelitz, F., Hall, E., 1949, Brit. Journal of Experimental Pathology, *30*:175–85). Eight of the 45 substances showed some activity against a few phages. Six of the 8 active substances were quinone compounds. The other 2 were polymixin B and viomycin.

Thirty-four of the 45 substances were also studied for their action against free phage particles. Ten different races of phage were used in this investigation. Twenty-two of the 34 substances were found to be capable of inactivating some free phage particles following 24 hours' exposure. These include several quinone compounds, patulin, subtilin, penicillic acid, polymixin B & D, streptomycin, neomycin, d-usnic acid, viomycin and aspergillic acid. 11 references. 2 figures. 5 tables.—*Author's abstract.*

157. *Role of Inhibitors and Mutations in Antibiotic Resistance by Escherichia Coli.* BURTON A. WAISBREN, CLAIRE CARR AND DAVID STRUXNESS, Minneapolis, Minn. Antibiotics and Chemotherapy *1*:534–39, November 1951.

Neomycin, polymyxin B, and Q-19 were three antibiotics whose *in vitro* antibac-

terial activity suggested possible clinical effectiveness against coliform organisms (4, 5, 6, 7). Thus it was of some importance to determine possible modes of resistance *E. coli* might have against these agents.

Escherichia coli exhibited a pattern of resistance to polymyxin B and Q-19 which was intermediate between the patterns usually found against penicillin and streptomycin, i.e., in a large population there were invariably some organisms moderately more resistant to polymyxin B and Q-19 than were the majority. *Escherichia coli* exhibited a pattern of resistance to neomycin of the "penicillin type," i.e., in a large population there was minimal variation in the sensitivities of the organisms.

Organisms resistant to polymyxin B that were found in cultures of *E. coli* were shown by the method of Luria and Delbrück to be true mutants.

A heat-stable filterable substance, which inhibited polymyxin B, Q-19 and neomycin, but did not effect aureomycin, streptomycin, penicillin, and chloramphenicol, remained after acetone and ether extraction of *E. coli*.

Mutants resistant to polymyxin B did not produce an increased quantity of the inhibitor substance. Therefore, the production of an inhibitor and mutation represent separate modes of resistance of *E. coli* to antibiotics. 16 references. 2 tables.—*Author's abstract.*

158. *Antibiotic Sensitivity Tests on Microaerophilic Bacteria and on Strains of Mycobacterium Tuberculosis Using Compressed Tablets.* ROBERT E. HOYT, Los Angeles, Calif. Antibiotics and Chemotherapy *1*:469–72, October 1951.

Compressed tablets containing antibiotic agents were utilized in indicating sensitivity of microaerophilic bacteria. The organisms were streaked on a plate of suitable media and covered by an overlay of thioglycollate agar. The testing tablets were placed on the surface of the overlay and the plate was incubated. Readings are made in the usual manner.

Suspension of a culture of *M. tuberculosis* was streaked on the surface of a Lowenstein's slant and a compressed tablet containing streptomycin was placed on the surface. Sensitivity was indicated by inhibition of growth around the tablet. A strain known to be resistant to 25 μg. streptomycin per ml. showed no inhibition. Inhibition did not occur when the tablets were added several days after inoculation, even though growth was not apparent at the time the tablets were introduced. 3 references. 2 figures.—*Author's abstract.*

159. *Classification of Six Hundred Salmonella and Shigella Strains Isolated from Patients of Cook County Hospital.* OSCAR FELSENFELD, VIOLA MAE YOUNG, AND TAMA YOSHIMURA, Chicago, Ill. *18*:209–12, July 1951.

Two hundred and eighty-six salmonella and 314 shigella strains from patients in the Cook County Hospital in Chicago were identified. The most frequently encountered salmonellae were (in decreasing order) *S. typhimurium*, *S. thyphosa*, *S. montevideo*, *S. oranienburg*, *S. newport*, *S. anatum*, *S. enteritidis* and *S. paratyphi* B, while often encountered shigellae were classified as *Sh. sonnei*, *Sh. paradysenteriae* Flexner IV, *Sh. alkalescens* and *Sh. paradysenteriae* Flexner II. The occurrence of

rare types is reported. There seemed to be a shift in the frequency of salmonella strains, as compared with previous studies in the same geographic area but the distribution of shigellae did not change. The importance of carriers and poultry in human salmonellosis was discussed. 20 references, 3 tables.—*Author's abstract.*

160. *The Resultant Sensitivity of Microorganisms to Various Antibiotics After Induced Resistance to Each of These Agents.* JACQUES J. MONNIER AND EMANUEL B. SCHOENBACH, Baltimore, Md. Antibiotics and Chemotherapy *1*:472–86, October 1951.

Resistance of organisms was induced to penicillin, aureomycin, chloramphenicol, terramycin and streptomycin by serial transfer in media containing one of these antibiotics. The microorganisms were then tested for their susceptibility to the antibiotic employed (direct acquisition of resistance) and also to the heterologous antibiotics to which they had not been directly exposed. The final sensitivity after subsequent transfer in nonantibiotic-containing media was also determined.

All organisms were found to acquire rapidly a permanent direct type of resistance to streptomycin. Tolerance to aureomycin and terramycin was induced with staphylococci and various Gram-negative bacilli. In streptococci, however, the resistance induced was slight and poorly maintained upon serial transfer in antibiotic-free media. Tolerance to chloramphenicol was readily acquired by Gram-negative bacilli, but not by Gram-positive cocci. Only a moderate degree of resistance to penicillin could be induced and this was of the temporary type. The susceptibility of the microorganisms which had been made resistant to penicillin was unchanged when tested with streptomycin or the other antibiotics. Among the Gram-negative bacilli, a parallel change in sensitivity was noted when they had been exposed to either aureomycin, chloramphenicol or terramycin and tested with each of the three antibiotics. The same relationship held with the Gram-positive cocci with aureomycin and terramycin, but not with chloramphenicol.

The susceptibility to polymyxin D was completely independent of alterations in sensitivity induced by the other antibiotics. Microorganisms which had been exposed to chloramphenicol, terramycin, aureomycin and streptomycin often showed increased sensitivity to penicillin and this was most marked in those strains initially found capable of forming penicillinase. The production of penicillinase appeared to be suppressed by exposure of microorganisms to these antibiotics, which was maintained through successive generations in which no antibiotic was present.

The biologic and clinical implications of these observations with respect to combination antibiotic therapy and laboratory procedures are discussed.—*Author's abstract.*

book reviews

Biological Antagonism. The Theory of Biological Relativity. GUSTAV J. MARTIN, Sc.D., Philadelphia, The Blakiston Company, 1951. Price: $8.50.

The many advances in the fields of biologic chemistry, pharmacology, immu-

nology, and other disciplines for which biochemical data is used have been faced, at one time or another, with the problem of antagonism in its broadest sense. Dr. Martin has attempted to integrate these observations with respect to enzyme chemistry, immunology, endocrinology, and even experimental chemotherapy into an over-all plan.

A tremendous amount of data has been collected and it must be said that the book verges on the encyclopedic. Unfortunately, however, unless one is well versed in the different disciplines, the premises or conclusions are sometimes difficult to understand.

This book will be of tremendous aid to those interested in the various aspects of biologic antagonism, ranging from metabolite analogues to the differential utilization of amino-acids in protein formation, sulfonamide antagonism, development of drug resistance, interference phenomena among viruses, etc. This information would be very difficult to obtain within the literature of any one field and should serve as a stimulus to the chemist, biologist, immunologist, bacteriologist, as well as the physician concerned with metabolic research.—*Emanuel B. Schoenbach, M.D.*

Acta Medica Scandinavica, supplement 263 (volume 140), 1951. Aseptic (Non-Bacterial) Encephalomeningitides in Gothenburg, 1932-1950. Clinical and Experimental Investigation with Special Reference to the Viruses of Herpes, Influenza, Mumps, and Lymphocytic Choriomeningitis. LESLIE AFZELIUS-ALM (from the Virus Department of the Bacteriological Laboratory, Sahlgren's Hospital, Gothenburg, Sweden).

With the development of modern virus techniques, the problem of aseptic lymphocytic meningitis has received a great deal of attention since the description by Wallgren. Many of these cases are being segregated into known etiologic classifications. However, from the symptomatic, clinical, and pathologic observations, little differential material is available.

The author has made a most extensive study of the cases observed in Gothenburg. *Encephalitis lethargica*, influenza, poliomyelitis, postvaccinal states, and similar types of central nervous system infection were excluded when possible. An epidemiologic survey revealed no seasonal incidence. There was a uniform attack rate from 1932 to 1950 except for an increased incidence in 1945 to 1947. No increase was noted in the number of cases during outbreaks of influenza, poliomyelitis, or mumps. It was found that 50 per cent of the children and 25 per cent of the adults had an associated upper respiratory infection. This was also true of 70 per cent of the patients who came to postmortem examination. Among children the chief signs were those of diffuse central nervous system involvement. In adults a paralysis of the lower cranial nerves was frequently seen. The over-all mortality rate was 6 per cent.

Clinical laboratory studies indicated that the outstanding change in the spinal fluid was a pleocytosis, in which lymphocytes predominated, without increase in cerebrospinal fluid pressure. There was no marked cytoalbuminuric dissociation.

Pathologically, the chief observation was hemorrhagic encephalitis (Hurst), generally involving the white matter of the brain and the brain stem.

Extensive laboratory studies were made and cerebrospinal fluid, brain, and blood were injected into mice, rabbits, and guinea pigs. Complement fixation and neutralizing antibodies were also measured. It is interesting to note that no tests were positive for lymphogranuloma virus or lymphocytic choriomeningitis. On a number of occasions the animals became ill with virus which was endemic to them rather than to the patients. Herpes virus, although difficult to incriminate in such diseases because only 21 per cent of the series had no antibodies at the onset, was found to play an important role in the cases of aseptic meningitis; 23 per cent of the group developed such antibodies following the infection.

As an extension of these studies, work was conducted at the Army Medical School among American troops and here too it was found that 54 per cent of the individuals with lymphocytic meningitis had no detectable antibody, and 21 per cent of the group developed such antibody. The over-all incidence of *herpes virus encephalitis* was 7 per cent. This observation is most unusual because the only recorded cases have been of patients who succumbed in the early phase of the disease. Clinically, it has always been felt that *herpes encephalitis* was far more common, but no evidence had been assembled to confirm this impression. It is also of interest to note that 8 per cent of the patients with lymphocytic meningitis were infected with mumps without evidence of glandular involvement. These data are quite different from that assembled in the United States where approximately 25 per cent of the cases of encephalitis were due to lymphocytic choriomeningitis, and 20–30 per cent to mumps.

This is an excellent study which is recommended to those interested in the problem of aseptic meningitides, the vast majority of which is still unexplained etiologically. The Coxsackie group of viruses was considered but no studies were performed in this Gothenburg series. There was no epidemiologic evidence for an epidemic variety of infection.—*Emanuel B. Schoenbach, M.D.*

Heart Disease: Its Diagnosis and Treatment. EMANUEL GOLDBERGER, B.S., M.D., Lea and Febiger, Philadelphia, 1951. Price: $10.00.

This text on heart disease has as its objective the presentation of data on the diagnosis and treatment of cardiovascular disease for the general practitioner. The aim has been well met in that it is well organized and clearly presented, the various terms are lucidly defined, there are numerous illustrations of the subject material, and special emphasis is placed on those procedures which aid in bedside diagnosis. The diseases for which helpful therapy is available are presented in greater detail than the esoteric or uncommon varieties. That Dr. Goldberger has apparently had wide personal experience in the treatment of various types of heart disease is evident in his exposition. The comparative lack of detail with respect to the physiologic principles or those subjects which are at present controversial has resulted in a very clear presentation of methods and procedures. The latter, however, are somewhat didactic and authoritative.

This book can be recommended to the family practitioner who wishes a clear and concise presentation of the problems originating primarily with dysfunction of the heart. However, medical students and internists probably would prefer a more stimulating presentation of the problems encountered in diseases of the cardiovascular system. An adequate bibliography is appended to each chapter although there is no reference to it in the text.—*Emanuel B. Schoenbach, M.D.*

Cancer Cytology of the Uterus. J. EARNEST AYRE, M.D., New York, Grune and Stratton, 1951. 442 pages, 362 illustrations, 79 in color. Price: $14.50.

One of the significant contributions to the early diagnosis of accessible neoplasms has been the introduction of the Papanicolaou technic for the recognition of cancer cells in secretions from various organs.

The monograph by Dr. J. Earnest Ayre has been beautifully prepared and is replete with clear illustrations, many of which are in color. The technical aspects of this monograph arouse one's admiration. In addition, there are sections on the technics employed which would certainly make this method of diagnosis valuable to all who are interested in the subject.

The conclusions, however, are unsupported except by short references and one wonders whether many of the refined classifications, such as nearo-carcinoma, etc., are truly valid. At this point, nevertheless, one could not ask for a clearer presentation of all the facets comprising this type of study. It is recommended to all who are interested in the early diagnosis of cervical cancer.—*Emanuel B. Schoenbach, M.D.*

Acta Medica Scandinavica, supplement 261 (volume 140), 1951. Renal Physiology in Electrolyte Subtraction. D. A. DENTON, VICTOR WYNN, I. R. MC DONALD AND SHIRLEY SIMON (from the Department of Physiology, Melbourne University, Australia).

The authors, employing the technic of electrolyte subtraction, which heretofore has been little used in renal physiology, have been able to collect a large mass of experimental data of great value. By studying electrolyte data from patients with the post-gastrectomy type of duodenal fistulae, they have been able to subtract from the body fluid containing twice as much sodium as chloride. It is shown that if Na^+ is subtracted from the body in excess of Cl^- relative to the extracellular ratio of these two ions, the ratio $\frac{Cl}{Na}$ in the extracellular fluid remains constant. This is because the kidney excretes Cl^- in excess of Na^+ commensurately with the stress.

By subjecting the excess gastric juice obtained from the patients postoperatively to electrolyte balance studies, the situation where excess Cl^- is subtracted was analyzed. It was found that during excess Cl^- subtraction, pattern control was achieved by renal excretion of Na^+ in excess of Cl^-. In these circumstances the kidney may not excrete Cl^- ion even though the plasma level is raised and Na^+ ion is simultaneously being concentrated in the urine.

Experiments conducted on sheep, using esophageal fistulae to produce excess Na^+ subtraction, also confirm the above conclusions.

The authors speculate that the renal tubules act as homeostatic regulators relative to an ionic pattern rather than to an absolute level of an individual factor. They therefore suggest that a terminology which involves absolute concepts (e. g. the "renal threshold" or Tm value of an electrolyte) may not be sufficiently adequate to describe the facts.—*Benjamin Rosenberg, M.D.*

The Clinical Use of Fluid and Electrolyte. JOHN H. BLAND, M.D. (from the University of Vermont College of Medicine). W. B. Saunders Company, Philadelphia, 1952. 259 pages, 75 illustrations. Price: $6.50.

This monograph on the problems of the chemical constitution of the body fluids, chiefly with respect to electrolyte contents, will be appreciated by internists and others concerned with the care of patients. The electrolyte shifts in disease which are associated with steroid or replacement therapy have achieved considerable importance during the past decades as more adequate methods for determination of electrolytes.

The presentations are clear and outlined with numerous biographic sketches so that the complex interrelationships of fluid and electrolyte shifts can easily be visualized. Anyone who has been concerned with the associated problems will find this monograph extremely useful, and there are adequate references for those who would like greater detail and substantiating descriptions.

Some of the headings will indicate the important phases of this problem which are covered: Water and Electrolyte in Congestive Heart Failure; Normal and Abnormal Potassium Metabolism; Water and Electrolyte in Pediatric Disease; Clinical Use of Fluid and Electrolyte in the Aged and Aging, Renal Disease, Diabetes Mellitus; and ACTH and Cortisone.—*Emanuel B. Schoenbach, M.D.*

The Battle for Mental Health. JAMES CLARK MOLONEY, M.D., Philosophical Library, New York, 1952. 98 pages. Price: $3.50.

The book is a rather compressed presentation of the author's views concerning the genesis and prophylaxis of present-day mental illness. An attempt to cover the subjects of a definition of mental health, statistics on mental illness in the United States, criticism of the "American way of life," discussion of primitive cultures, emotional needs of infants, defects of maternity hospitals, motivation of obstetricians, nurses and mothers, in addition to a plea for the "permissive method" of raising children and the advantages of the "rooming-in" arrangement for the newborn results in a kaleidoscopic presentation of facts, arguments and subject material. The variety of topics combined with lack of organization and the failure to balance the importance of the various subjects results in an impression that the work represents notes in outline from which many volumes may be written in the future. There is too much statistical data for the layman and insufficient documentation for the physician, sociologist or psychologist.

There are many intriguing ideas presented which are thought-provoking and novel. One may cite the effect on medical practice in the United States that the pre-eminence of the German school of medicine exerted during the latter part of the nineteenth century and early years of the twentieth century as an example. Not only the scientific and professional accomplishments were brought back by postgraduate students but also elements of the Germanic social system of rigidity and strict conformity in behavior. It is hoped that the subject of mental health as envisioned by Dr. Moloney will be expanded in the future into a larger volume with greater opportunity to expand upon the various concepts so succinctly presented at this time.—*Emanuel B. Schoenbach, M.D.*

Teratomas. RUPERT A. WILLIS, D.SC., M.D., F.R.C.P., Leeds, England. Atlas of Tumor Pathology, Section III, Fascicle 9, Published by the Armed Forces Institute of Pathology, Washington, D. C., 1951. 58 pages, 45 figures. Price: 50 cents.

The teratomas have been treated in this volume separately from the malignant tumors of the testes previously discussed. All one can say at this time is that the problem has been well presented. There is a short discussion on nomenclature, classification, incidence, knowledge as to the origin, and the gross and microscopic appearance of the various benign and malignant teratomas.

The monograph is a very valuable addition to the series on tumor pathology.—*Emanuel B. Schoenbach, M.D.*

Tumors of the Breast. FRED W. STEWARD, M.D., New York, N. Y. Atlas of Tumor Pathology, Section IX, Fascicle 34, Published by the Armed Forces Institute of Pathology, Washington, D. C., 1951. 114 pages, 68 illustrations. Price: $1.10.

This contribution to the Atlas of Tumor Pathology is probably one of the most outstanding presentations of the subject the reviewer has ever seen. The classification and prognostic implications are clearly defined and the illustrations are noteworthy for their quality and educational detail. The critical presentation of the text material with personal observations is one of the unusual and desirable features.

Because of the high incidence of tumors in the breast I am sure that every physician will wish to have this informative monograph at hand.—*Emanuel B. Schoenbach, M.D.*

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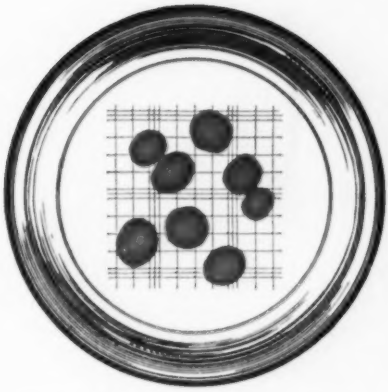

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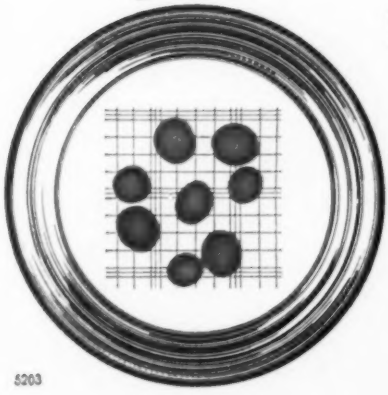

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